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IAN022: Clinical signs

EXPERIMENTAL PROCEDURE

ANIMAL SUPPLY

Donor animals

Transgenic piglets were selected from litters produced by the Sponsor under Project Licence No. PPL [redacted] Transgenic piglets supplied for the study were 7 - 21 days old and their weights in the range 2 to 3 kg.

Recipient animals

Captive-bred cynomolgus monkeys (*Macaca fascicularis*) were selected from shipments of animals bred at [redacted]. They were imported through a UK commercial supplier [redacted]. Their age at transplantation was 19 months to 31 months and their weights in the range 1.9 to 3.7 kg.

The animals used in this study were selected from stock held on behalf of the Sponsor to undergo screening as suitable recipients. Based on the results of the prescreening investigations, animals were selected by the Sponsor for transplant (see PRE-OPERATIVE INVESTIGATIONS). Whilst animals of either sex were selected, there was no specific requirements to maintain a balanced sex-ratio, as other selected criteria were more important. Only data relating to those animals that underwent transplant is present in this report.

ANIMAL MANAGEMENT

Piglets

On the day of transplant, selected animals were delivered to Huntingdon Life Sciences by the Sponsor.

Cynomolgus monkeys

All animals were conditioned in England for at least 4 weeks before delivery to the Huntingdon Life Sciences. Documentation received from the supplier included details relating to quarantine dates, health screening and any treatment administered during the conditioning period. On arrival at HRC they were examined by a Veterinary Officer and allocated a unique colony number, which was tattooed under the right arm. Intrapalpebral tuberculin tests were performed at intervals of approximately 6 weeks, beginning soon after arrival, but tests were not performed in the week prior to planned laboratory investigations. For transplanted animals, due to the frequency of planned laboratory investigations and by virtue of the fact that these animals were immunosuppressed, intrapalpebral tuberculin testing was stopped following transplant.

The animals were housed individually in cages specifically designed to house non-human primates in clean and secure conditions and which were in compliance with the Home Office Code of Practice for the Housing and Care of Animals used in Scientific Procedures. Prior to transplant the animals were housed in one of two different cage types, commonly known as 'metal' and 'printboard' cages. Metal cages were constructed of aluminium and electro-polished stainless steel and incorporated a squeeze-back system, perch, food hopper, bottle holders and a 2.5 × 2.5 cm grid floor. The cages were entirely wall-mounted in two tiers, each tier combined with an excreta removal flushing system which was cleaned twice daily. The cages were changed at intervals of approximately 4 weeks. Printboard cages were constructed of a stainless steel framework and 'printboard' walls, shelves and ceiling, incorporating a squeeze-back system, wooden perch, food hopper, water bottle holder and a removable 2.5 × 2.5 cm grid floor. Under the front half of each cage was a removable tray which contained wood chippings for use as a litter/forage substrate. The cages were cleaned and the litter replaced each day. Automatic drinking valves, for the supply of drinking water, were used for both types of cage and checked each day.

Following transplant, the animals were housed in 'printboard' cages. When considered practicable, transplanted animals were housed with a non-transplanted partner. It was recognised that the pairing of animals might be beneficial to the continued post-operative recovery and long-term survival.

The rooms in which the animals were kept were as far as practicable isolated from external disturbances. The room temperature was maintained in the range 19 to 25°C, using heat exchangers connected to hot water supplied from oil-fuelled boilers. Relative humidity was maintained in the range 48 to 85%. The environment was governed by a computer controlled building management system which continuously monitored the temperature and humidity controls and the operational state of the air handling plant. Temperature and relative humidity were recorded using a Rototherm Recorder. Deviations in temperature and/or humidity outside the set limits were generally due to the use of fan heaters as supplementary heat sources and when water was used to wash-down cages and/or floors. Artificial lighting was used and was controlled to give 12 hours of light and 12 hours of dark per 24 hours. Air extraction was via a balanced system designed to give fifteen air changes per hour.

FOOD AND WATER

Prior to transplant cynomolgus monkeys were each offered 150 or 200 grams of standard dry diet [redacted] daily, depending on the type of caging in which they were housed (150 g × 'printboard' cages; 200 g 'metal' cages). Following transplant all animals were offered 150 grams, of which 50 grams was occasionally replaced by TrioMunch. Animals housed in metal cages were generally fed twice daily, receiving 100 grams in the morning and a further 100 grams in the afternoon. Animals housed in printboard cages were offered the full ration in the morning. All animals were starved overnight prior to surgery.

Water was available at all times. Vitamin C (Blackcurrant [redacted] and [redacted] (a vitamin B_{12} preparation, [redacted]) were added to the drinking water on one day of each week.

There was no information available to the Study Director to indicate that any non-nutrient substance likely to influence the effect of the test substance could reasonably be expected to be present in the diet or the drinking water, both of which are routinely subjected to chemical analysis. Results of all the analyses were lodged in the Huntingdon Life Sciences Archives (Huntingdon).

Wholemeal bread and fresh fruit or vegetable produce was sometimes offered in order to enrich the environment and improve the interaction between the animals and their handlers.

STUDY DESIGN

All animals were considered on an individual basis. A total of 61 animals underwent heterotopic abdominal cardiac xenotransplantation. Of these, 4 animals also received transplants of foetal pig islets, either placed under the renal capsule or in an omental sac. The Sponsor was responsible for categorising the reasons why animals were sacrificed (*ie* technical failure, xenograft rejection).

All animals that underwent transplant received immunosuppressive treatment with a combination of [redacted]

Details of donor-recipient pairings for transplants undertaken and the dates on which they were performed are listed in Appendix 1. All recipient animals were identified by their unique HRC colony number.

The study was designed such that all animals initially followed a standard immunosuppressive protocol prior to and immediately following transplant. After a few days the immunosuppressive regime was then individually tailored for each animal, being based on the results of the laboratory investigations and blood drug levels. Details of the immunosuppressive regimes applied to individual animals are presented in Appendix 3. The initial dosing regimes are summarised as follows:

[redacted] was initially administered by intramuscular injection at a dosage of [redacted] Animals were dosed in this manner in the morning, typically from Day [redacted] In the first instance [redacted] was used (animals receiving transplants on 13, 14, 27 and 28 March 1995). Due to adverse reactions at the injections sites, [redacted] was subsequently used for the rest of the study (animals receiving transplants on or after 2 May 1995). Oral administration of [redacted] generally commenced by [redacted] at differing dosages specified by the Sponsor. The required dosage of [redacted] was given as a split dose in the morning and late afternoon/early evening.

[redacted] was initially administered by intravenous injection on Day [redacted] at a dosage of [redacted] and again on Days [redacted] and [redacted] at a dosage of [redacted]. Subsequently oral administration of [redacted] generally commenced on Day [redacted] at a dosage of [redacted] and on alternate days thereafter or as required at the discretion of the Sponsor.

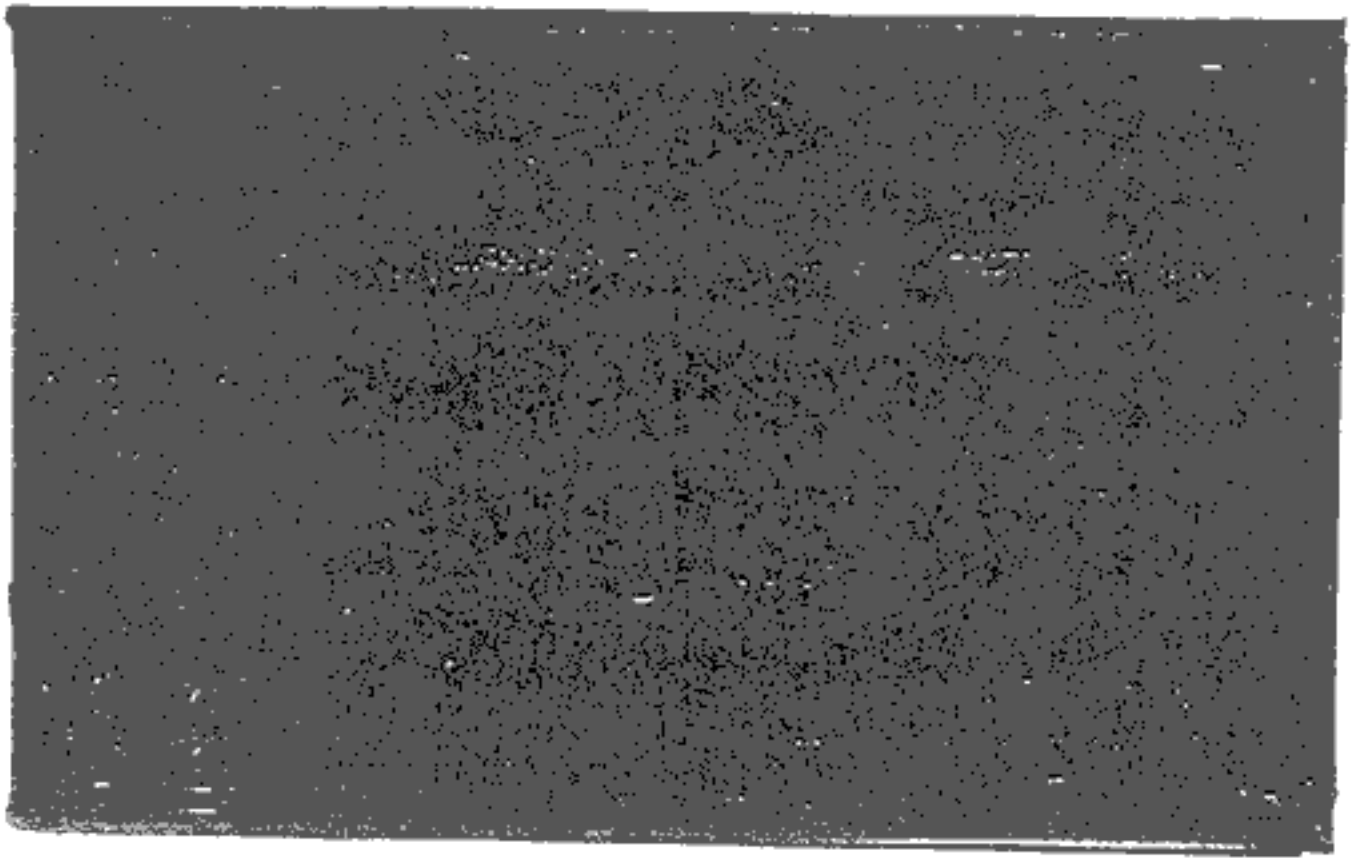
[redacted] was administered by intravenous injection at a dosage of [redacted] at the time of transplant (Day 0). Animals were then dosed orally with [redacted] at the same dosage level on Days [redacted] and [redacted] after which the dosage level was reduced daily by [redacted] increments until a dosage of [redacted] was reached. Thereafter animals were maintained at that dosage level.

Transplant operations were performed on 2 or 3 recipient animals per day and were spread over a period of several months, dependent on the availability of surgeons. The commencement of the study for these subgroups were therefore varied, dependent on when the transplant was performed.

The animals were housed in the [redacted]

PREPARATION OF THE TEST SUBSTANCES

The test substances were prepared for administration as follows:



ADMINISTRATION OF THE TEST SUBSTANCES

The animals were dosed at approximately the same time(s) each day when applicable. Individual doses were adjusted according to the most recent bodyweight. The required quantity of each test solution was measured into a suitably graduated plastic syringe.

For oral dosing the test solutions were administered through a plastic catheter inserted via the mouth into the stomach. The catheter was flushed through with a small quantity (5-10 ml) of (a high carbohydrate, low electrolyte, low fluid drink;).

For intravenous administration, the test solution was injected using a infusion set inserted into the cephalic or saphenous vein.

For intramuscular administration the test solution was injected through an appropriate gauge hypodermic needle. The animal was dosed in the thigh, the hair having been removed by clipping, to facilitate administration and to observe any local reaction to the injection.

Intravenous administration of steroid on the day of transplant was carried out during surgery. The dose was administered through an indwelling cannula inserted into a peripheral vein (ie saphenous).

FORMULATION SAMPLING

The pharmaceutical preparations used in this study were for the treatment of animals to prevent the rejection of a transplanted transgenic organ. With the exception of [redacted] these materials were all licensed pharmaceutical products.

Details of batch usage were documented and records of the daily preparation and administration of formulations were maintained. It was therefore not considered necessary that formulation samples be taken for analysis of achieved concentration.

PRE-OPERATIVE INVESTIGATIONS

During the acclimatisation period, blood samples were obtained from potential recipient animals for various investigations to enable the selection of the most compatible donor-recipient pairings. Blood samples, were obtained for the following investigations.

Huntingdon Life Sciences

1. Pre-transplant haematology and biochemistry

Imutran Limited

2. Anti-pig antibody titres)
3. CH50) (10 ml into plain tubes)
4. Blood group)

Investigations carried out on donor animals were the responsibility of the Sponsor and as such, have been documented and reported separately.

Prior to transplant (Day -1) and again on the day of transplant, blood samples (1 ml whole blood) were taken for measurement of C-peptide, for those animals scheduled also to receive a foetal islet transplant. A further blood sample (100 µl into Alsevers solution) was taken for flow cytometry analysis of mononuclear subsets.

SURGICAL PROCEDURE (including anaesthetic management)

Recipient animals

All animals were starved overnight prior to surgery. Prior to transfer to the operating theatre the animal was sedated with [redacted] given by the intramuscular route in combination with [redacted] injection, [redacted].

Following induction of anaesthesia by intravenous injection of [redacted] an endotracheal tube was inserted and the animals were maintained on a [redacted] mixture, with the addition of [redacted] at a concentration of [redacted] as required.

Prophylactic antibiotic therapy was given [redacted].

An indwelling cannula was inserted into a peripheral vein for administration of fluids and drugs etc during the procedure. The animal was transferred to the operating table where appropriate respiratory and electrocardiographic monitoring was established.

The abdominal skin was then prepared with aqueous based Betadine solution, and sterile drapes applied to expose the operative field. A midline laparotomy was then performed and the abdominal viscera gently retracted to allow exposure of the abdominal aorta and inferior vena cava at a level below the renal arteries. These vessels were prepared to receive the vascular anastomoses of the donor heart and rubber slings were passed around the vessels to isolate them. At this stage there was a pause in the recipient operation to allow removal and preparation of the donor heart. Gauze swabs soaked in saline were applied to the abdominal contents to maintain a moist environment and the abdominal wound retractor removed.

Following removal and preparation of the donor heart the recipient animals abdominal wound was re-opened and the previously prepared vessels exposed. Vascular clamps were applied to the aorta and vena cava proximal and distal to the planned site of the anastomoses. A longitudinal venotomy and arteriotomy was made to allow direct end to side suture of the donor pulonary artery and aorta to the recipient vena cava and aorta respectively. Standard microvascular suture techniques were used. On completion of the anastomoses and before the sutures were finally tied the vessels were flushed with heparinised saline and back bleeding and forward flush techniques used to ensure that there was no thrombotic material within any of the vessels. After this flush the vascular clamps were removed to reperfuse the transplanted heart and the time recorded. Tissue glue [redacted] was placed around the anantomoses. The animal also received an intravenous injection of [redacted].

For those animals that also received transplants of foetal pig islets, the following procedures also applied.

Following cardiac xenotransplantation and prior to closure of the abdomen, pieces of foetal pig pancreas were transplanted under the capsule of both left and right recipient kidneys. Both kidneys were visualised and a small opening made in the renal capsule at the posterior pole. A metal probe was introduced into the opening to made a tunnel by separating the capsule from the underlying renal cortex. A purse-string suture was made around the opening.

The pancreas fragments, prepared and supplied by the Sponsor, were placed in a 5 ml plastic syringe with 16G plastic tubing attached. The plastic tubing was inserted into the pocket and the pancreas pieces extruded as the tubing was withdrawn. The opening to the pocket was closed by tying the suture. The intention was to infiltrate approximately 50 to 100 pancreas pieces over a tract of approximately 2 cm, which should subsequently be clearly visible through the kidney capsule.

Alternatively, an omental pocket was created in the greater omentum. This structure was exteriorised and spread out over a moist pack. A wide purse-suring suture was made so that a pocket was created into which the islets were placed. The suture was then tied so that the islets were enclosed in the pouch which was then replaced into the abdominal cavity.

For all animals, once the surgeon was satisfied that there was stable xenograft function and adequate haemostasis was observed the abdominal wound was closed and the recipient allowed to recover from general anaesthesia. The animal was then returned to its cage.

Donor animals

During the preparation of the recipient, the donor animal was sedated with [redacted] Initial induction of anaesthesia was by inhalation via a face mask and following transfer to the operating table, endotracheal intubation via tracheostomy was performed to allow mechanical ventilation.

The thoracic skin was prepared and draped to expose the operative field and a median sternotomy was performed to expose the intra-throacic organs. The sternal halves were separated by a retractor and a thymectomy performed to allow better access to the pericardium, which was opened in the midline. At this stage the pig was heparinised systemically by direct injection of sodium heparin [redacted] into the superior vena cava. Dissection was performed to mobilise the heart and great vessels, passing slings around the intra-pericardial inferior vena cava (IVC), the superior vena cava (SVC), and the ascending aorta. The azygos vein was isolated and divided between ligatures as it entered the posterior aspect of the IVC. At this stage the heart was adequately mobilised for removal.

The ascending aorta was then cross clamped and cold crystalloid cardioplegic solution administered into the aortic route to institute cardioplegic arrest with exsanguination for the animal through the IVC and inferior pulmonary veins which were cut to allow drainage. After arrest was established the heart was excised by dividing in turn the IVC, left inferior and superior pulmonary veins, the left and right pulmonary arteries; the SVC and finally the ascending aorta. The heart was then transferred to a bowl containing cold saline and prepared for implantation.

After inspection for a patent foramen ovale, and creation of an atrio-septal defect if one was not present, the IVC and SVC were sutured closed. Next the back wall of the left atrium was prepared and the orifices of the pulmonary veins obliterated. The heart was then transferred to a bowl containing cold saline and prepared for implantation.

POST-OPERATIVE MANAGEMENT

Recipient animals were closely monitored for the first 24 hours post-operation.

Post-operative analgesia was provided by the use of [redacted] which was administered at the discretion of the attending veterinary surgeon. Other drugs may have been prescribed if considered appropriate. Details of individual drug administrations were recorded in the study records.

Animals received a single administration of [redacted] on the day prior to transplant. From Day 1, a single dose was given daily (or more frequently if considered necessary) at the discretion of the attending veterinarian. Animals received a subcutaneous dose at a dosage of [redacted]

Dependent on the clinical condition of each animal, food and/or fluid supplements were given at the discretion of the attending veterinary surgeon and/or Sponsor's monitoring scientist (or their deputy). Also, heat lamps were used to warm the animals until such time their use was no longer required, as determined by the attending HRC veterinarian.

In the event of any animal showing a deterioration in it's clinical condition, heat lamps were used at the discretion of the attending HRC veterinarian.

POST-OPERATIVE OBSERVATIONS

Dated and signed records of all activities relating to the day by day running and maintenance of the study within the animal unit, as well as to the group observations and examinations outlined in this protocol, were recorded in the Study Day Book. In addition, observations relating to individual animals made throughout the day were recorded.

The following observations were made during the course of the study:

Mortality

The circumstances of any death was recorded in detail and a full *post mortem* examination was performed as described later. Prior to death, observations listed in this protocol were carried out, where practicable.

Clinical signs

All signs of ill health or reaction to treatment was recorded. Animals were checked regularly throughout the working day from approximately 0800 to 1700 hours (including weekends and public holidays).

The animals were removed from their cages at regular intervals to assess their general condition and to palpate the transplanted heart to check for cardiac activity (see POST-OPERATIVE INVESTIGATIONS).

Bodyweight

The bodyweight of all animals was recorded weekly during the pre-transplant period and daily during the post-operative period. The animals were weighed in the morning prior to dosing, or at a similar time during the pre-transplant period.

Food consumption

Although the quantity of food (standard dry diet) left by individual animals together with an estimate of the quantity spilled was recorded on a daily basis throughout the experimental period, animals also had access to varying amounts and types of supplements. Consequently the quantities of diet consumed have not been reported.

POST-OPERATIVE INVESTIGATIONS

Xenograft function and physical examination

The functioning of the xenograft was determined at least three times each day for the first 2 weeks following transplant and then twice daily. Thereafter xenograft function was checked more frequently at the discretion of the Study Director and/or HRC veterinary staff. A check of the general physical condition of the animal was also performed at the same time.

If it was not possible to observe the xenograft functioning whilst the animal was in its cage, the animal was removed from its cage and the xenograft palpated, if necessary.

At these occasions additional treatments *ie* topical applications to wound, analgesics etc, were given to the animal as prescribed or directed by HRC's veterinarian or the Sponsor's representatives.

Blood sampling

Following transplant, blood samples were obtained from all surviving animals on Mondays, Wednesdays and Fridays. Blood samples were taken in the morning prior to any dosing. For individual animals, the frequency of the various investigations and the parameters measured were occasionally amended at the Sponsor's request on the basis of the animal's clinical condition or previous results.

For animals that also received foetal islet transplants, additional blood samples (100 µl into Alsevers solution and 250 µl whole blood) were taken at the same times as the scheduled investigations, for assay of C-peptide and flow cytometry analyses.

(a) Laboratory investigations performed at HRC

Haematology and biochemistry investigations were performed as follows:

Haematology	Units
300 µl into 0.5 ml EDTA tube. The following investigations were performed with an Ortho ELT-1500 haematology analyser	
Packed cell volume (PCV)	%
Haemoglobin (Hb)	g/dl
Red blood cell count (RBC)	$\times 10^6/mm^3$
Total white cell count (WBC Total)	$\times 10^3/mm^3$
Platelet count (Plts)	$\times 10^3/mm^3$

	Units
Differential WBC count	
Neutrophils (N) Lymphocytes (L) Eosinophils (E) Basophils (B) Monocytes (M)	$\times 10^3/mm^3$
Cell Morphology : If definitely abnormal cells were observed when examining any stained slide, such as the presence of Heinz bodies or abnormal lymphocytes etc, their presence or absence on each such slide examined was recorded and tabulated separately.	
Biochemistry	
700 µl into heparinised microtainer. The following parameters were analysed with a Hitachi 737 Clinical Chemistry analyser	
* Urea	mg/dl
Creatinine (Creat)	mg/dl
Sodium (Na)	mEq/l
Potassium (K)	mEq/l
Calcium (Ca)	mEq/l
Inorganic Phosphorus (P)	mEq/l
Chloride (Cl)	mEq/l
* Total Bilirubin (Bilirubin)	mg/dl
* Osmolality (Osmol) - using a Wescor vapour pressure osmometer	mOsm/kg
The following parameters were analysed using a Roche Cobas Centrifugal analyser, using the appropriate BCL test kit:	
*Glutamic pyruvic transaminase (GPT), also known as 'Alanine aminotransferase' Reaction temperature 30°C	mU/ml
*Glutamic-oxaloacetic transaminase (GOT), also known as 'Aspartate aminotransferase' Reaction temperature 30°C	mU/ml
*Leucine amino peptidase (LAP) Reaction temperature 30°C	mU/ml

Units

The following parameter was analysed as described:

*Ornithine Carbamoyltransferase (OCT) - Method of Ceriotti, G. (*Clin. Chim. Acta.* 1973, 47, 97)
Reaction temperature 37°C — mU/ml

- These parameters were only investigated for individual animals if indicated by their clinical condition and as recommended by the Sponsor or attending Veterinarian.

(b) **Blood samples for despatch to** [redacted] **or** [redacted]

Anti-pig antibody levels

0.5 ml into plain tube. Samples were analysed at [redacted]

[redacted] **levels**

0.2 ml into 0.5 ml EDTA tube. Samples were analysed at [redacted]

Biopsy of pancreatic islet graft sites

Thirteen days following transplant a biopsy sample of the foetal islet graft sites was taken from W401m. Under general anaesthesia a small incision was made in the abdomen. The graft site was biopsied by a small superficial wedge incision in the graft, after opening the kidney capsule. Haemostasis was achieved by cautery and the incision reclosed over a small piece of gelatin foam to achieve tamponade. The biopsy specimen was placed in Bouin's fixative prior to despatch to the Sponsor for examination.

TERMINAL STUDIES

The animals were maintained and dosed according to the immunosuppressive protocol unless sacrifice was required due to one of the following events occurring.

1. rejection of xenograft, as defined by absence of palpable cardiac activity.

2. opportunistic infection, as a result of the immunosuppressive treatment. Any signs of infection was brought to the attention of HRC veterinary staff and was treated symptomatically as considered necessary. In the event of an animal developing an infection that could not be treated, the animal was sacrificed following authorisation by the attending veterinarian.

3. drug toxicity, arising from the immunosuppressive treatment. Regular monitoring of the animals both clinically and by blood sampling minimised the risk of drug toxicity.

The Sponsor was contacted before any decision was taken to sacrifice an animal.

Pre-terminal blood sampling

Prior to sacrifice as much blood as practicable was collected and divided appropriately into heparinised and plain blood tubes.

Following centrifugation the plasma/serum was separated and deep frozen (in cardice) prior to despatch to the Sponsor for analysis.

Necropsy procedure

Each animal was immobilised with [redacted] given by the intramuscular route. The animals were then killed by a lethal dose of [redacted] and then rapidly exsanguinated by incision of the carotid blood vessels.

Immediately after exsanguination the xenograft with its associated anastomoses was carefully removed and weighed. A small section from the wall of each of the four chambers was taken and placed on a cork disc, covered in OCT-embedding matrix [redacted] and rapidly frozen in liquid nitrogen. Each section was then individually wrapped in foil and stored deep frozen (in cardice) prior to despatch to the Sponsor.

The remainder of the transplanted heart, with the exception of samples for virus studies (see below), was placed in neutral-buffered formalin.

Additionally, where applicable, a small biopsy sample of the foetal islet graft site was placed in Bouin's fixative. The remainder of the kidney or omental sac was placed in neutral buffered formalin. These samples were despatched to the Sponsor for examination.

Virus studies

Samples of the following tissues were required to be taken from all recipient animals where the cardiac xenograft had survived in excess of 5 days. The size of the sample taken was ideally approximately 0.5 cm^3 or if this size was not possible, as much was feasible. The following tissue samples were taken:

- transplanted heart
- vascular anastomoses (junction or donor pulmonary artery and aorta and recipient vena cava and aorta)
- lining of abdominal cavity that had been in contact with the transplanted heart
- kidney
- heart (recipient)
- lung
- liver
- ovaries or testes
- pancreas
- brain
- ileum
- mid-colon

For individual animals where other tissue samples were taken at the discretion of the Sponsor's Monitoring Scientist, these have been documented in the study records.

All samples were snap frozen in liquid nitrogen and stored deep frozen in cardice prior to despatch to Imutran.

LOCATION OF STUDY RECORDS

All specimens (except those sent to the Sponsor or other third party), raw data and other documents generated at Huntingdon Life Sciences, together with a copy of the final report were lodged in the Huntingdon Life Sciences, Archives, Huntingdon, England.

Such specimens and records were retained for a minimum period of five years from the date of issue of the final report. At the end of the five year retention period the Client will be contacted and advice sought on their future requirements. Under no circumstances will any item be discarded without the Client's knowledge.

Data arising from any investigations made by the Sponsor or other third party, the findings of which are included in the Huntingdon Life Sciences final report, was retained and archived by the Sponsor.

PROCEDURES

The procedures used during the study, with the exception of the anaesthesia, biopsy and surgical procedures, were documented in the relevant Huntingdon Life Sciences Procedures Manuals.

DEVIATIONS FROM PROTOCOL

There were no deviations from protocol other than those documented in the study records and which related to the clinical management of individual animals on a day-to-day basis.

APPENDIX 9

Clinical signs

Explanatory notes

Clinical signs are reported from the day following transplant (Day 1) and therefore do not include those animals that did not return from surgery on the day of transplant, or those that were subsequently sacrificed on Day 0.

The clinical signs presented in this Appendix are only the first and last observations reported for each day the animal survived. Due to the frequent and numerous procedures performed on the animals throughout the course of each day, the signs displayed by them other than first thing in the morning or last thing in the evening, were considered to be unrepresentative of the underlying clinical condition of each animal.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W142f	1	AM	Alert, reasonably active.
		PM	Alert, reasonably active.
	2	AM	Quiet, but alert.
		PM	Quiet, but alert.
	3	AM	Alert and active.
		PM	Alert and active.
	4	AM	Alert and active.
		PM	Alert and active.
	5	AM	Loose faeces. Quiet but alert.
		PM	Loose faeces. Quiet but alert.
	6	AM	Loose faeces. Alert and reasonably active.
		PM	Sacrificed.
W141m	1	AM	Alert and active.
		PM	Alert and active.
	2	AM	Quiet but alert.
		PM	Quiet but alert.
	3	AM	Alert and active.
		PM	Alert and active.
	4	AM	Alert and active.
		PM	No comment made on condition of animal.
	5	AM	Quiet, alert.
		PM	Quiet, alert.
	6	AM	Quiet, alert.
		PM	Quiet, alert.
	7	AM	Alert and active.
		PM	Alert and active.
	8	AM	Alert and active.
		PM	Alert and active.
	9	AM	Alert and active.
		PM	Alert and active.
	10	AM	Alert and active.
		PM	Alert and active.
	11	AM	Quiet but alert.
		PM	Alert and active.
	12	AM	Alert and active.
		PM	Alert and active.
	13	AM	Alert and active.
		PM	Alert and active.
	14	AM	Alert and active.
		PM	Alert and active.
	15	AM	Alert and active.
		PM	Alert and active.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W141m (continued)	16	AM	Alert and active.
		PM	Alert and active.
	17	AM	Alert and active.
		PM	Alert and active.
	18	AM	Quiet but alert.
		PM	Quiet but alert.
	19	AM	Alert and active.
		PM	Alert and active.
	20	AM	Alert and active. Loose faeces.
		PM	Alert and active. Loose faeces.
	21	AM	Alert and active. Possible vomit/liquid faeces in tray.
		PM	Alert and active.
	22	AM	Alert and active.
		PM	Quiet but alert.
	23	AM	Alert and active.
		PM	Alert and active.
	24	AM	Quiet but alert.
		PM	Quiet but alert.
	25	AM	Quiet but alert.
		PM	Quiet but alert.
	26	AM	Quiet but alert.
		PM	Quiet but alert.
	27	AM	Alert and active.
		PM	Alert and active.
	28	AM	Alert and active.
		PM	Alert and active.
	29	AM	Quiet but alert.
		PM	Quiet but alert.
	30	AM	Quiet but alert. Vomit post dosing
		PM	Quiet but alert.
	31	AM	Quiet but alert.
		PM	Quiet but alert. Loose faeces.
	32	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	33	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	34	AM	Quiet, huddled. Loose faeces.
		PM	Quiet, huddled. Unsteady when moving. Sacrificed
W140f	1	AM	Alert and active.
		PM	Alert and active.
	2	AM	Alert and active.
		PM	Alert and active.
	3	AM	Alert and active.
		PM	Alert and active.
	4	AM	Alert and active.
		PM	No comment made on condition of animal.
	5	AM	Alert and active.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W140f	5	PM	Alert and active.
(continued)	6	AM	Alert and active.
		PM	Alert and active.
	7	AM	Alert and active.
		PM	Alert and active.
	8	AM	Alert and active.
		PM	Alert and active.
	9	AM	Alert and active.
		PM	Alert and active.
	10	AM	Alert and active.
		PM	Alert and active.
	11	AM	Quiet but alert.
		PM	Alert and active.
	12	AM	Alert and active.
		PM	Alert and active.
	13	AM	Alert and active.
		PM	Alert and active.
	14	AM	Alert and active.
		PM	Alert and active.
	15	AM	Alert and active.
		PM	Alert and active.
	16	AM	Alert and active.
		PM	Alert and active.
	17	AM	Alert and active.
		PM	Alert and active.
	18	AM	Quiet but alert.
		PM	Quiet but alert.
	19	AM	Alert and active.
		PM	Alert and active.
	20	AM	Alert and active. Loose faeces.
		PM	Alert and active.
	21	AM	Alert and active. Possible vomit/liquid faeces in tray.
		PM	Alert and active.
	22	AM	Quiet but alert.
		PM	Quiet but alert.
	23	AM	Alert and active.
		PM	Alert and active.
	24	AM	Quiet but alert.
		PM	Quiet but alert.
	25	AM	Quiet but alert.
		PM	Quiet but alert.
	26	AM	Quiet but alert.
		PM	Quiet but alert
	27	AM	Alert and active.
		PM	Alert and active.
	28	AM	Alert and active.
		PM	Alert and active.
	29	AM	Quiet but alert.
		PM	Quiet but alert. Loose faeces.
	30	AM	Quiet but alert.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W140f	30	PM	Quiet but alert.
(continued)	31	AM	Quiet but alert.
		PM	Quiet but alert. Loose faeces.
	32	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	33	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	34	AM	Quiet, huddled. Loose faeces.
		PM	Quiet, huddled.
	35	AM	Sacrificed.
W135m	1	AM	Alert, reasonably active.
		PM	Alert, reasonably active.
	2	AM	Alert and active.
		PM	Alert and active.
	3	AM	Alert and active.
		PM	Alert and active.
	4	AM	Alert and active.
		PM	Alert and active.
	5	AM	Alert and active.
		PM	Alert and active.
	6	AM	Alert and active.
		PM	Alert and active.
	7	AM	Alert and active. Possible vomit/liquid faeces in tray.
		PM	Alert and active.
	8	AM	Alert and active.
		PM	Quiet but alert.
	9	AM	Alert and active. Loose faeces.
		PM	Alert and active. Loose faeces.
	10	AM	Quiet but alert.
		PM	Quiet but alert.
	11	AM	Quiet but alert.
		PM	Quiet but alert.
	12	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	13	AM	Alert and active.
		PM	Alert and active.
	14	AM	Alert and active. Loose faeces.
		PM	Alert and active. Loose faeces.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W135m (continued)	15	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	16	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. No loose faeces.
	17	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	18	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	19	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	20	AM	Alert and active. Loose faeces.
		PM	Alert and active.
	21	AM	Quiet but alert. Loose/liquid faeces. Vomit post dosing
		PM	Alert and active.
	22	AM	Alert and active. Some loose faeces.
		PM	Quiet but alert.
	23	AM	Alert and active.
		PM	Alert and active. No faeces seen.
	24	AM	Alert and active. Normal faeces.
		PM	Alert and active.
	25	AM	Dark faeces.
		PM	Dark faeces.
	26	AM	Alert and active. Dark loose/liquid faeces.
		PM	Alert and active. No faeces seen.
	27	AM	Alert and active. Loose/normal faeces.
		PM	Alert and active. No faeces seen.
	28	AM	Alert and active. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	29	AM	Alert and active. Loose faeces.
		PM	Alert and active. No faeces seen.
	30	AM	Alert and active. Loose/liquid faeces.
		PM	Alert and active. Dark loose faeces.
	31	AM	Alert and active. Dark loose faeces.
		PM	Quiet but alert. Liquid faeces.
	32	AM	Alert and active. Loose faeces.
		PM	Alert and active. No faeces seen.
	33	AM	Alert and active.
		PM	Alert and active. Watery vomit.
	34	AM	Alert and active.
		PM	Alert and active.
	35	AM	Alert and active. Loose faeces.
		PM	Alert and active. Loose faeces.
	36	AM	No comment made on condition of animal.
		PM	Quiet but alert. Liquid faeces.
	37	AM	Quiet but alert. Liquid faeces.
		PM	Quiet but alert. No faeces seen. Sacrificed.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W143m	1	AM	Quiet but alert. Slightly unsteady.
		PM	Quiet but alert.
	2	AM	Alert. No faeces seen.
		PM	Alert. No faeces seen.
	3	AM	Alert and active. No faeces seen.
		PM	Alert and active. Faeces seen.
	4	AM	Alert and active.
		PM	Alert and active.
	5	AM	Alert and active.
		PM	Alert and active.
	6	AM	Alert and active.
		PM	Alert and active.
	7	AM	Alert and active. Loose/liquid faeces.
		PM	Alert and active. Loose/liquid faeces.
	8	AM	Alert and active. Normal faeces.
		PM	Alert and active. Vomit
	9	AM	Alert and active.
		PM	Alert and active.
	10	AM	Alert and active.
		PM	No comment made on condition of animal.
	11	AM	Alert and active.
		PM	No comment made on condition of animal.
	12	AM	Alert and active.
		PM	Alert and active.
	13	AM	Alert and active.
		PM	Alert and active.
	14	AM	(Records not available)
		PM	(Records not available)
	15	AM	(Records not available)
		PM	(Records not available)
	16	AM	(Records not available)
		PM	(Records not available)
	17	AM	(Records not available)
		PM	(Records not available)
	18	AM	(Records not available)
		PM	(Records not available)
	19	AM	(Records not available)
		PM	(Records not available)
	20	AM	(Records not available)
		PM	(Records not available)
	21	AM	Alert and active.
		PM	Alert and active.
	22	AM	Alert and active.
		PM	Alert and active.
	23	AM	Alert and active.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W143m	23	PM	Alert and active.
(continued)	24	AM	Alert and active.
		PM	Alert and active.
	25	AM	Alert and active.
		PM	Alert and active.
	26	AM	Alert and active.
		PM	Alert and active.
	27	AM	Alert and active.
		PM	Alert and active.
	28	AM	Alert and active.
		PM	Alert and active.
	29	AM	Alert and active.
		PM	Alert and active.
	30	AM	Alert and active.
		PM	Alert and active.
	31	AM	Alert and active.
		PM	Alert and active.
	32	AM	Alert and active.
		PM	Alert and active.
	33	AM	Alert and active. Loose faeces.
		PM	Alert and active. Loose faeces.
	34	AM	Alert and active. Loose faeces.
		PM	Alert and active. No faeces seen.
	35	AM	Alert and active.
		PM	Alert and active.
	36	AM	Alert and active.
		PM	Alert and active.
	37	AM	Alert and active.
		PM	Alert and active.
	38	AM	Alert and active.
		PM	Alert and active.
	39	AM	Alert and active. Quiet.
		PM	Alert and active. Quiet.
	40	AM	Alert and active.
		PM	Alert and active.
	41	AM	Alert and active.
		PM	Alert and active.
	42	AM	Alert. Dark faeces.
		PM	Alert. Dark faeces.
	43	AM	Alert. Loose faeces. Sneezing.
		PM	Alert. Sneezing. No loose faeces seen.
	44	AM	Alert and active. Dark faeces.
		PM	Alert and active. No faeces seen.
	45	AM	Alert and active. Loose faeces.
		PM	Alert and active. Loose faeces.
	46	AM	Alert and active. Loose faeces.
		PM	No faeces seen.
	47	AM	Alert and active. No loose faeces seen.
		PM	Alert and active.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W143m (continued)	48	AM	Alert and active. Dark faeces.
		PM	Alert and active. Dark faeces.
	49	AM	Alert and active. Dark faeces.
		PM	Quiet but alert. Dark faeces.
	50	AM	Alert and active. Dark faeces.
		PM	Alert and active. Normal faeces.
	51	AM	Alert and active.
		PM	Alert and active.
	52	AM	Alert and active.
		PM	Alert and active. Dark faeces.
	53	AM	Quiet but alert.
		PM	Quiet but alert.
	54	AM	Quiet but alert. Loose faeces.
		PM	Sacrificed.
W328f	1	AM	Alert and active.
		PM	Alert and active.
	2	AM	Alert and active.
		PM	Alert and active.
	3	AM	Alert and active.
		PM	Alert and active.
	4	AM	Alert and active.
		PM	Alert and active.
	5	AM	Alert and active.
		PM	Alert and active.
	6	AM	Alert and active.
		PM	Alert and active. Some loose faeces.
	7	AM	Alert and active. Loose/liquid faeces.
		PM	Alert and active. No faeces seen.
	8	AM	Quiet. Liquid faeces.
		PM	Appears more alert. Loose faeces.
	9	AM	Quiet. Loose faeces.
		PM	Quiet, alert.
	10	AM	Quiet. Loose faeces.
		PM	Quiet. Normal faeces.
	11	AM	Quiet. Loose faeces.
		PM	Quiet. Loose faeces.
	12	AM	Quiet but alert. Liquid faeces.
		PM	Quiet but alert. Liquid faeces.
	13	AM	Quiet but alert. Loose/liquid faeces.
		PM	Liquid faeces.
	14	AM	Quiet but alert. Loose faeces.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W328f	14	PM	Quiet but alert. Loose faeces.
(continued)	15	AM	Alert and active. Loose faeces.
		PM	Alert and active. Loose faeces.
	16	AM	Alert and active. Liquid faeces.
		PM	No faeces passed.
	17	AM	Alert and active. Liquid faeces.
		PM	Alert and active. Loose faeces.
	18	AM	Alert and active. Loose faeces.
		PM	Alert and active. Loose faeces.
	19	AM	Alert and active. Small amount of loose faeces.
		PM	Alert and active. Small amount of loose faeces.
	20	AM	Alert and active. Loose faeces.
		PM	Alert and active. No faeces seen.
	21	AM	Quiet but alert. Dark loose/liquid faeces.
		PM	Quiet but alert. No faeces seen.
	22	AM	Alert and active. Loose/normal faeces.
		PM	Alert and active. Loose faeces.
	23	AM	Alert and active. Loose/normal faeces.
		PM	Alert and active. Loose/normal faeces.
	24	AM	Quiet but alert. Loose/normal faeces.
		PM	Quiet but alert. Loose/normal faeces.
	25	AM	Quiet but alert. Loose/normal faeces.
		PM	Quiet but alert. Loose/normal faeces.
	26	AM	Quiet but alert. Liquid faeces.
		PM	No faeces seen.
	27	AM	Quiet, little movement. Pale liquid faeces.
		PM	Quiet, little movement. No faeces seen.
	28	AM	Quiet, huddled. Loose and pale faeces.
		PM	Quiet but alert. No faeces passed.
	29	AM	Quiet, huddled. Loose faeces.
		PM	Quiet but alert. Liquid faeces.
	30	AM	Quiet but alert. Loose and pale liquid faeces.
		PM	Quiet, huddled. Pale liquid faeces.
	31	AM	Quiet, huddled. Pale liquid faeces.
		PM	Quiet but alert. Pale loose/liquid faeces.
	32	AM	Quiet but alert. No loose faeces seen.
		PM	Alert. No faeces seen.
	33	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	34	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert.
	35	AM	Quiet but alert.
		PM	Quiet but alert.
	36	AM	Quiet but alert.
		PM	Quiet but alert.
	37	AM	Quiet but alert.
		PM	Quiet. Liquid faeces.
	38	AM	Quiet. Liquid faeces.
		PM	Quiet but alert. Liquid faeces.
	39	AM	Alert and active. Dark liquid faeces.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W328f	39	PM	Quiet but alert.
(continued)	40	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	41	AM	Quiet but alert. Normal faeces.
		PM	Quiet but alert.
	42	AM	Quiet but alert.
		PM	Quiet but alert.
	43	AM	Quiet but alert.
		PM	Quiet but alert. Pale loose/liquid faeces.
	44	AM	Quiet but alert. Pale loose faeces.
		PM	Quiet but alert.
	45	AM	Quiet but alert. Loose faeces.
		PM	Quiet, huddled. No loose faeces seen. Liquid and food vomit.
	46	AM	Quiet but alert. No loose faeces seen.
		PM	No comment made on condition of animal.
	47	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Normal faeces.
	48	AM	Quiet but alert. No loose faeces seen.
		PM	Quiet but alert.
	49	AM	Quiet but alert. Loose faeces.
		PM	Quiet. Loose faeces.
	50	AM	Quiet but alert. Pale loose faeces.
		PM	Quiet but alert. No loose faeces seen.
	51	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Vomit in tray. No loose faeces seen.
	52	AM	Quiet but alert. Pale loose faeces.
		PM	Quiet but alert. Pale loose faeces.
	53	AM	Quiet but alert. Liquid faeces. Semi digested diet vomit.
		PM	Quiet but alert. Liquid faeces.
	54	AM	Quiet but alert. Liquid faeces. Semi digested diet vomit in tray.
		PM	Quiet but alert. Liquid faeces.
	55	AM	Quiet but alert. Liquid faeces.
		PM	Quiet but alert. No faeces seen.
	56	AM	Quiet but alert. Liquid faeces.
		PM	Quiet, huddled, appears asleep. Loose faeces.
	57	AM	Quiet, huddled, reluctant to move. Loose/liquid faeces.
		PM	Sacrificed.
W323m	1	AM	Quiet, huddled.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W323m	1	PM	Quiet, more alert.
(continued)	2	AM	Quiet, huddled.
		PM	Quiet, huddled. Vomit in cage (fruit, clear and yellow fluid).
	3	AM	Quiet, huddled.
		PM	Quiet, more active. No faeces passed.
	4	AM	Quiet, reasonably alert.
		PM	Quiet, reasonably alert.
	5	AM	Quiet but alert.
		PM	Quiet but alert.
	6	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	7	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	8	AM	Alert and active. Normal faeces.
		PM	Alert and active. Large amount of fruit/watery vomit
	9	AM	Alert and active.
		PM	Alert and active.
	10	AM	Quiet but alert.
		PM	Alert and active.
	11	AM	Quiet but alert Small vomit.
		PM	Quiet but alert.
	12	AM	Alert and active.
		PM	Alert and active.
	13	AM	Alert and active.
		PM	Alert and active.
	14	AM	Alert and active at times. Some loose faeces.
		PM	Alert and active at times. Normal faeces.
	15	AM	Alert and active. Loose faeces.
		PM	Alert and active. No loose faeces seen.
	16	AM	Quiet but alert.
		PM	Quiet but alert.
	17	AM	Quiet but alert.
		PM	Quiet but alert.
	18	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	19	AM	Quiet but alert.
		PM	Quiet but alert.
	20	AM	Quiet but alert.
		PM	Quiet but alert.
	21	AM	Quiet, huddled. Dark faeces.
		PM	Quiet, huddled. Loose faeces.
	22	AM	Quiet, huddled. Dark loose faeces.
		PM	Quiet, huddled. Dark faeces.
	23	AM	Active and alert. Loose faeces.
		PM	Huddled but active and alert. Loose faeces.
	24	AM	Quiet but alert. Loose faeces.
		PM	Quiet, huddled. Loose faeces.
	25	AM	Quiet, huddled, piloerection. Little movement. Liquid faeces.
		PM	Quiet, huddled. Loose faeces.
	26	AM	Quiet, huddled. Loose faeces. Liquid faeces.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W323m	26	PM	Quiet, huddled. Normal faeces.
(continued)	27	AM	Quiet, huddled. Loose faeces.
		PM	Quiet, huddled. Loose faeces.
	28	AM	Quiet, huddled, very slow movement, eyes puffy. Dark faeces.
		PM	Sacrificed.
W326f	1	AM	No comment made on condition of animal.
		PM	Quiet.
	2	AM	Quiet but alert.
		PM	Quiet but alert.
	3	AM	Alert and active.
		PM	Alert and active.
	4	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Normal faeces.
	5	AM	Quiet but alert.
		PM	Quiet but alert.
	6	AM	Quiet but alert. Dark faeces.
		PM	Quiet but alert. Dark faeces.
	7	AM	Alert and active. Dark faeces.
		PM	Alert and active. Normal faeces.
	8	AM	Alert and active. Dark faeces.
		PM	Alert and active. Normal faeces.
	9	AM	Quiet but alert.
		PM	Quiet but alert.
	10	AM	Quiet but alert.
		PM	Alert and active.
	11	AM	Alert and active. Loose faeces.
		PM	Quiet but alert. Normal faeces.
	12	AM	Alert and active. Loose faeces.
		PM	Quiet but alert, huddled. No faeces seen.
	13	AM	Alert and active. Normal faeces.
		PM	Alert and active.
	14	AM	Alert and active.
		PM	Alert and active.
	15	AM	Quiet but alert.
		PM	Quiet but alert.
	16	AM	Alert and active.
		PM	Alert and active.
	17	AM	Alert and active.
		PM	Alert and active.
	18	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert.
	19	AM	Quiet but alert. Sneezing. Normal faeces.
		PM	Quiet but alert. Sneezing.
	20	AM	Quiet but alert.
		PM	Quiet but alert.
	21	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Normal faeces. Small vomit post dose.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W326f (continued)	22	AM	Quiet but alert.
		PM	Quiet but alert.
	23	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. No loose faeces seen.
	24	AM	Quiet but alert. Slight salivation post dose
		PM	Quiet, huddled.
	25	AM	Alert and active. Loose faeces.
		PM	No faeces seen
	26	AM	Alert and active. Loose faeces.
		PM	Alert and active. No faeces seen.
	27	AM	Alert and active. Some dark faeces.
		PM	Quiet, appears asleep.
	28	AM	Quiet but alert. Loose faeces. Small vomit post dose.
		PM	Quiet but alert. Loose faeces.
	29	AM	Alert and active. Loose faeces.
		PM	Alert and active. Loose faeces.
	30	AM	Alert and active. Dark faeces.
		PM	Alert and active. Normal faeces.
	31	AM	Alert and active. Loose faeces.
		PM	Quiet but alert. No loose faeces seen.
	32	AM	Quiet but alert. Loose/liquid faeces.
		PM	No comment made on condition of animal.
	33	AM	Quiet but alert. Loose/liquid faeces.
		PM	No comment made on condition of animal.
	34	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. No faeces seen.
	35	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. No loose faeces seen.
	36	AM	Quiet, huddled but alert. Liquid faeces.
		PM	Quiet, huddled but alert. No faeces seen.
	37	AM	Quiet, huddled. Loose faeces.
		PM	Quiet but alert. No loose faeces seen.
	38	AM	Quiet, huddled. Loose faeces.
		PM	Quiet but alert. No faeces seen.
	39	AM	Quiet but alert. Loose faeces.
		PM	Quiet, huddled. No faeces seen.
	40	AM	Quiet but alert. Normal faeces.
		PM	Quiet but alert.
	41	AM	Quiet but alert.
		PM	Quiet but alert. No faeces seen.
	42	AM	Quiet, huddled. Normal faeces.
		PM	Quiet, huddled, eyes slightly puffy. No faeces seen.
	43	AM	Quiet, huddled, eyes slightly puffy. Normal faeces.
		PM	Quiet, huddled, eyes slightly puffy.
	44	AM	Quiet, huddled, eyes slightly puffy. Loose/liquid faeces.
		PM	Quiet, huddled, eyes slightly puffy. Loose/liquid faeces.
	45	AM	Quiet, huddled, eyes slightly puffy. Loose/liquid faeces
		PM	Quiet, heavy lidded, huddled. Loose faeces.
	46	AM	Sacrificed.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W341m	1	AM	Quiet but alert. No faeces seen.
		PM	Quiet but alert. No faeces seen.
	2	AM	Quiet but alert. Normal faeces.
		PM	Quiet but alert.
	3	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Normal faeces.
	4	AM	Quiet but alert.
		PM	Quiet but alert.
	5	AM	Quiet but alert. Dark faeces.
		PM	Quiet but alert. Dark faeces.
	6	AM	Quiet but alert. Dark faeces.
		PM	Quiet but alert. Dark faeces. Vomit (5 - 8 ml) in tray.
	7	AM	Quiet but alert. Dark faeces.
		PM	Quiet but alert. No faeces seen.
	8	AM	Quiet but alert. Normal faeces.
		PM	Quiet but alert. Large vomit of diet/drug.
	9	AM	Quiet but alert.
		PM	Alert and active.
	10	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Normal faeces.
	11	AM	Alert and active. Loose faeces.
		PM	Alert, huddled. No faeces seen.
	12	AM	Alert and active. Normal faeces.
		PM	Alert and active.
	13	AM	Alert and active.
		PM	Alert and active.
	14	AM	Quiet but alert.
		PM	Quiet but alert.
	15	AM	Alert and active.
		PM	Alert and active.
	16	AM	Alert and active.
		PM	Quiet but alert.
	17	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert.
	18	AM	Quiet but alert. Normal faeces.
		PM	Quiet but alert.
	19	AM	Quiet but alert.
		PM	Quiet but alert.
	20	AM	Alert and active.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W341m	20	PM	Alert and active.
(continued)	21	AM	Quiet but alert.
		PM	Quiet but alert.
	22	AM	Quiet but alert.
		PM	Quiet but alert.
	23	AM	Quiet but alert.
		PM	Quiet, huddled.
	24	AM	Alert and active. Loose faeces.
		PM	Alert and active. Loose faeces.
	25	AM	Alert and active. Loose faeces.
		PM	Alert and active. No faeces seen.
	26	AM	Quiet but alert. Dark faeces.
		PM	Quiet but alert, appears asleep.
	27	AM	Huddled, appears asleep. Loose faeces.
		PM	Quiet, huddled. Liquid faeces.
	28	AM	Quiet, huddled. No loose faeces seen.
		PM	Quiet, huddled. Loose faeces.
	29	AM	Quiet but alert. No loose faeces seen.
		PM	Quiet.
	30	AM	Quiet but alert. Eyes slightly puffy. Dark faeces.
		PM	Quiet but alert. Eyes slightly puffy. Normal faeces.
	31	AM	Quiet, huddled.
		PM	Quiet, huddled, eyelids heavy. No faeces seen.
	32	AM	Quiet, huddled. Eyes slightly puffy.
		PM	Quiet, huddled. Eyes slightly puffy.
	33	AM	Quiet, huddled. Eyes and muzzle slightly puffy. Little movement.
		PM	Quiet, huddled. Eyes and muzzle slightly puffy. Little movement. Dark faeces.
	34	AM	Quiet, huddled. Eyes slightly puffy. Loose/liquid faeces. Small vomit (1 - 2 ml) of Hycal.
		PM	Quiet, huddled. No faeces seen.
	35	AM	Quiet, huddled. Eyes slightly puffy. Slightly dark faeces. Prepuce swollen.
		PM	Quiet, huddled. Eyes slightly puffy. Slightly dark faeces. Prepuce swollen.
	36	AM	Quiet, huddled. Eyes slightly puffy. Pale loose faeces. Prepuce swollen.
		PM	Quiet, huddled. Eyes slightly puffy. Liquid faeces. Prepuce swollen.
	37	AM	Quiet, huddled. Eyes slightly puffy. Pale loose faeces.
		PM	Quiet, huddled. Eyes slightly puffy. Dark liquid faeces.
	38	AM	Quiet, huddled. Eyes slightly puffy. Loose faeces.
		PM	Quiet, huddled. Normal faeces.
	39	AM	Quiet, huddled. Eyes slightly puffy. Loose/dark faeces.
		PM	Quiet. Eyes slightly puffy. No faeces seen.
	40	AM	Quiet, huddled. Eyes slightly puffy. Loose faeces.
		PM	Quiet, huddled. Eyes slightly puffy. No faeces seen.
	41	AM	Quiet, huddled. Eyes slightly puffy. Normal faeces.
		PM	Quiet, huddled. Eyes slightly puffy.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W341m (continued)	42	AM	Quiet, huddled. Eyes slightly puffy.
		PM	Quiet, huddled. Eyes slightly puffy.
	43	AM	Quiet. Eyes slightly puffy. Loose faeces.
		PM	Quiet, huddled. Normal faeces.
	44	AM	Quiet but alert. Loose/liquid faeces.
		PM	Quiet. No loose faeces seen.
	45	AM	Quiet, huddled.
		PM	Quiet, huddled.
	46	AM	Quiet, huddled. Loose faeces.
		PM	Quiet, huddled. Loose faeces.
	47	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. No faeces seen.
	48	AM	Quiet, huddled. Normal faeces.
		PM	Quiet, huddled.
	49	AM	Quiet, huddled.
		PM	Quiet but alert.
	50	AM	Quiet, huddled.
		PM	Quiet, huddled.
	51	AM	Quiet, huddled.
		PM	Quiet, huddled. Loose faeces.
	52	AM	Quiet, huddled. Loose/liquid faeces.
		PM	Quiet, huddled. Loose/liquid faeces.
	53	AM	Quiet, huddled. Liquid faeces.
		PM	Quiet, huddled. Liquid faeces.
	54	AM	Quiet, huddled. Loose faeces.
		PM	Quiet but alert. No loose faeces seen.
	55	AM	Quiet but alert.
		PM	Quiet but alert.
	56	AM	Quiet, huddled.
		PM	Quiet, huddled.
	57	AM	Quiet, huddled. Pale liquid faeces. Some blood stained mucus in loose pale faeces.
		PM	Quiet, huddled. No faeces seen.
	58	AM	Quiet, with occasional active periods. Pale loose faeces.
		PM	Quiet, with occasional active periods. No loose faeces seen.
	59	AM	Quiet, huddled.
		PM	Quiet, huddled.
	60	AM	Quiet, huddled
		PM	Quiet, huddled.
	61	AM	Quiet, huddled, little movement.
		PM	Sacrificed.
W374f	1	AM	Quiet but alert.
		PM	Quiet but alert.
	2	AM	Quiet but alert.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
374f	2	PM	Quiet but alert.
(continued)	3	AM	Quiet but alert.
		PM	Quiet but alert.
	4	AM	Quiet but alert.
		PM	Alert and active.
	5	AM	Alert and active. Dark faeces.
		PM	Quiet but alert. Active.
	6	AM	Alert and active.
		PM	Alert.
	7	AM	Alert and active.
		PM	Alert and active.
	8	AM	Sacrificed.
W333m	1	AM	Alert and active.
		PM	Quiet but alert.
	2	AM	Alert and active.
		PM	Alert and active.
	3	AM	Alert and active.
		PM	Alert and active.
	4	AM	Alert and active. Dark faeces.
		PM	Alert and active. Quiet.
	5	AM	Alert and active.
		PM	Alert.
	6	AM	Alert and active.
		PM	Alert and active.
	7	AM	Alert and active. Loose faeces.
		PM	Alert and active. Normal faeces.
	8	AM	Quiet but alert.
		PM	Quiet but alert.
	9	AM	Alert and active.
		PM	Alert and active.
	10	AM	Alert and active.
		PM	Alert and active.
	11	AM	Alert and active.
		PM	Alert and active.
	12	AM	Alert and active.
		PM	Alert and active.
	13	AM	Alert and active. Dark faeces.
		PM	Alert and active.
	14	AM	Alert and active. Normal faeces.
		PM	Alert and active.
	15	AM	Alert and active.
		PM	Alert and active.
	16	AM	Alert and active.
		PM	Alert and active.
	17	AM	Alert and active.
		PM	Alert and active.
	18	AM	Alert and active.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W333m	18	PM	Alert and active.
(continued)	19	AM	Alert and active.
		PM	Alert and active.
	20	AM	Alert and active.
		PM	Alert and active.
	21	AM	Alert and active.
		PM	Alert and active.
	22	AM	Alert and active.
		PM	Alert and active. Dark faeces.
	23	AM	Alert and active. Dark faeces.
		PM	Alert and active. Dark faeces.
	24	AM	Alert and active.
		PM	Alert and active.
	25	AM	Quiet but alert. Loose faeces.
		PM	No abnormalities detected.
	26	AM	Alert and active. No loose faeces seen.
		PM	No abnormalities detected.
	27	AM	Quiet but alert. Loose faeces.
		PM	Quiet, huddled. No loose faeces seen.
	28	AM	Quiet but alert.
		PM	Quiet but alert.
	29	AM	Alert and reasonably active.
		PM	Quiet, huddled.
	30	AM	Quiet, huddled but alert. Loose faeces.
		PM	Quiet, huddled. No faeces seen.
	31	AM	Quiet, huddled but alert. Loose faeces.
		PM	Quiet, huddled but alert. Loose faeces.
	32	AM	Quiet, huddled but alert. Loose faeces.
		PM	Alert and active. No loose faeces seen.
	33	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	34	AM	Quiet but alert. Normal faeces.
		PM	Quiet, huddled. No faeces seen.
	35	AM	Quiet, huddled. Normal faeces.
		PM	Quiet, huddled.
	36	AM	Quiet, huddled.
		PM	Quiet, huddled.
	37	AM	Quiet, huddled.
		PM	Quiet, huddled.
	38	AM	Quiet but alert, coughing.
		PM	Quiet but alert.
	39	AM	Quiet, huddled. Puffy around eyes.
		PM	Quiet, huddled. Puffy around eyes.
	40	AM	Quiet but alert. Puffy around eyes.
		PM	Quiet but alert, more active. Puffy around eyes.
	41	AM	Quiet but alert, huddled. Puffy around eyes.
		PM	Quiet but alert, huddled. Puffy around eyes.
	42	AM	Quiet, huddled. Slightly puffy eyes.
		PM	Quiet, huddled.
	43	AM	Quiet but alert. Slightly puffy eyes.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W333m	43	PM	Quiet, huddled.
(continued)	44	AM	Quiet but alert. Eyes normal.
		PM	Quiet but alert.
	45	AM	Quiet but alert. Normal faeces.
		PM	Quiet but alert.
	46	AM	Quiet but alert.
		PM	Quiet but alert.
	47	AM	Quiet but alert.
		PM	Quiet but alert.
	48	AM	Quiet but alert.
		PM	Quiet but alert.
	49	AM	Alert and active.
		PM	Alert and active.
	50	AM	Alert and active.
		PM	Alert and active.
	51	AM	Alert and active.
		PM	Alert and active.
	52	AM	Alert and active. Loose faeces.
		PM	Quiet but alert. No loose faeces seen.
	53	AM	Alert and active. No faeces seen.
		PM	Alert and active.
	54	AM	Alert and active. Normal faeces.
		PM	Alert and active.
	55	AM	Alert but quiet.
		PM	Sacrificed.
W438f	1	AM	Quiet but alert. No faeces seen
		PM	Quiet but alert. No faeces seen
	2	AM	Alert and active. Normal faeces.
		PM	Alert and active.
	3	AM	Alert and active.
		PM	Alert and active.
	4	AM	Alert and active.
		PM	Alert and active.
	5	AM	Alert and active.
		PM	Alert and active.
	6	AM	Alert and active. Loose faeces. Semi digested diet vomit.
		PM	Alert and active. No loose faeces seen.
	7	AM	Alert and active.
		PM	Alert and active.
	8	AM	Alert and active. Liquid faeces.
		PM	Alert and active. No loose faeces seen.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W438f (continued)	9	AM	Alert and active. Loose faeces.
		PM	Alert and active. Loose faeces.
	10	AM	Alert and active. Loose faeces.
		PM	No comment made on condition of animal.
	11	AM	Alert and active. No loose faeces seen.
		PM	No comment made on condition of animal.
	12	AM	Alert and active.
		PM	Alert and active.
	13	AM	Alert and active. Loose faeces.
		PM	Alert and active. Loose faeces.
	14	AM	Alert and active.
		PM	Alert and active.
	15	AM	Alert and active. Loose faeces.
		PM	Alert and active. No loose faeces seen.
	16	AM	Alert and active. Loose faeces.
		PM	Alert and active. Loose faeces.
	17	AM	Alert and active. Loose faeces.
		PM	Alert and active. No loose faeces seen.
	18	AM	Alert and active. Loose faeces.
		PM	Alert and active. No faeces seen.
	19	AM	Alert and active. Loose faeces.
		PM	Alert and active. Normal faeces.
	20	AM	Alert and active.
		PM	Alert and active.
	21	AM	Alert and active. Loose faeces.
		PM	Alert and active. No faeces seen.
	22	AM	Alert and active. Normal faeces.
		PM	Quiet but alert.
	23	AM	Alert and active.
		PM	Alert and active.
	24	AM	Alert and active.
		PM	Alert and active.
	25	AM	Quiet, huddled. Loose faeces.
		PM	Quiet, huddled. Loose faeces.
	26	AM	Alert and active. Normal faeces.
		PM	Alert and active.
	27	AM	Alert and active.
		PM	Biopsy performed under anaesthesia. Initially asleep, subsequently awake but unsteady. Sutures intact.
	28	AM	Quiet, huddled.
		PM	Quiet but alert.
	29	AM	Quiet but alert.
		PM	Quiet but alert.
	30	AM	Quiet but alert.
		PM	Alert.
	31	AM	Quiet but alert. Dark faeces.
		PM	Quiet, active. Normal faeces.
	32	AM	Quiet but alert. Dark faeces.
		PM	Quiet but alert. Dark faeces.
	33	AM	Quiet but alert. Dark faeces.
		PM	Alert and active. No faeces seen.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W438f (continued)	34	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	35	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. No loose faeces seen.
	36	AM	Quiet but alert. Pale/loose faeces.
		PM	Quiet but alert. No loose faeces seen.
	37	AM	Alert and active.
		PM	Alert and active.
	38	AM	Alert and active.
		PM	Alert and active.
	39	AM	Alert and active.
		PM	Alert and active.
	40	AM	Quiet but alert.
		PM	Quiet but alert.
	41	AM	Quiet but alert.
		PM	Quiet but alert.
	42	AM	Alert and active.
		PM	Sacrificed.
W401m	1	AM	Alert. No faeces seen.
		PM	Quiet, huddled. Little movement.
	2	AM	Alert. Gentle activity.
		PM	Alert and active.
	3	AM	Alert and active.
		PM	Alert and active.
	4	AM	Alert and active.
		PM	Alert and active.
	5	AM	Alert and active.
		PM	Alert and active.
	6	AM	Alert and active.
		PM	Quiet, huddled. Appears alert.
	7	AM	Alert and active.
		PM	Alert and active.
	8	AM	Quiet but alert.
		PM	Quiet but alert.
	9	AM	Alert and active.
		PM	Alert and active.
	10	AM	Quiet but alert.
		PM	Quiet but alert.
	11	AM	Quiet but alert and active.
		PM	Quiet but alert and active.
	12	AM	Quiet but alert.
		PM	Quiet but alert.
	13	AM	Quiet but alert.
		PM	Recovering from biopsy.
	14	AM	Quiet, huddled but alert.
		PM	Quiet, huddled but alert.
	15	AM	Quiet, huddled but alert.
		PM	Quiet but alert.
	16	AM	Quiet but alert.
		PM	Quiet but alert.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W401m (continued)	17	AM	Quiet but alert.
		PM	Quiet but alert.
	18	AM	Quiet but alert.
		PM	Quiet but alert.
	19	AM	Quiet but alert.
		PM	Quiet but alert.
	20	AM	Quiet, huddled but alert.
		PM	Quiet but alert.
	21	AM	Quiet but alert.
		PM	Quiet but alert.
	22	AM	Quiet but alert.
		PM	Quiet but alert.
	23	AM	Quiet but alert.
		PM	Quiet but alert.
	24	AM	Quiet but alert.
		PM	Quiet but alert.
	25	AM	Quiet but alert.
		PM	Quiet but alert.
	26	AM	Quiet but alert.
		PM	Quiet but alert.
	27	AM	Quiet but alert.
		PM	Quiet but alert.
	28	AM	Quiet but alert.
		PM	Quiet but alert.
	29	AM	Quiet but alert.
		PM	Quiet but alert.
	30	AM	Quiet, huddled.
		PM	Quiet.
	31	AM	Quiet, huddled.
		PM	Quiet, huddled. Puffiness around both eyes.
	32	AM	Quiet but alert. Swelling around eyes.
		PM	Quiet but alert. Swelling around eyes.
	33	AM	Quiet, huddled but alert. Puffiness around both eyes.
		PM	Quiet, huddled but alert. Puffiness around both eyes.
	34	AM	Quiet but alert. Swelling around both eyes. Loose faeces.
		PM	Quiet, huddled. Swelling around both eyes.
	35	AM	Quiet but alert. Swelling around both eyes. Loose faeces. Slightly unsteady.
		PM	Quiet but alert. Swelling around both eyes. Loose faeces. Slightly unsteady.
	36	AM	Quiet but alert. Swelling around both eyes. Slightly unsteady.
		PM	Sacrificed.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W409m	1	AM	Quiet but alert. Small amount of faeces seen.
		PM	Quiet but alert. No faeces seen.
	2	AM	Quiet but alert. No faeces seen.
		PM	Quiet but alert. Normal faeces
	3	AM	Alert and active.
		PM	Alert and active.
	4	AM	Quiet but alert.
		PM	Quiet but alert.
	5	AM	Alert and active. Interest shown in supplements.
		PM	Alert and active. Interest shown in supplements.
	6	AM	Alert and active.
		PM	Alert and active.
	7	AM	Alert and active.
		PM	Alert and active.
	8	AM	Alert and active.
		PM	Alert and active.
	9	AM	Alert and active.
		PM	Alert and active.
	10	AM	Alert and active.
		PM	Alert and active.
	11	AM	Alert and active.
		PM	Alert and active.
	12	AM	Alert and active.
		PM	Alert and active.
	13	AM	Alert and active.
		PM	Alert and active.
	14	AM	Alert and active. Loose faeces.
		PM	Alert and active.
	15	AM	Alert and active.
		PM	Alert and active.
	16	AM	Quiet but alert.
		PM	Sacrificed.
W544f	1	AM	Quiet but alert. No faeces seen.
		PM	Quiet but alert.
	2	AM	Quiet but alert.
		PM	Quiet but alert.
	3	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. No faeces seen.
	4	AM	Quiet but alert. No faeces seen.
		PM	Alert and active. No faeces seen.
	5	AM	Quiet but alert.
		PM	Quiet but alert. No faeces seen.
	6	AM	Alert and active.
		PM	Alert and active.
	7	AM	Alert and active.
		PM	Alert and active.
	8	AM	Alert and active.
		PM	No abnormalities detected.
	9	AM	Alert and active.
		PM	Alert and active.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W544f (continued)	10	AM	No abnormalities detected.
		PM	No abnormalities detected.
	11	AM	No abnormalities detected.
		PM	No abnormalities detected.
	12	AM	No abnormalities detected.
		PM	No abnormalities detected.
	13	AM	No abnormalities detected.
		PM	No abnormalities detected.
	14	AM	No abnormalities detected.
		PM	No abnormalities detected.
	15	AM	No abnormalities detected.
		PM	No abnormalities detected.
	16	AM	No abnormalities detected.
		PM	No abnormalities detected.
	17	AM	No abnormalities detected.
		PM	Small infection at operation site.
	18	AM	No abnormalities detected.
		PM	No abnormalities detected.
	19	AM	Dark faeces.
		PM	Dark faeces.
	20	AM	Dark faeces.
		PM	No faeces seen.
	21	AM	No abnormalities detected.
		PM	No abnormalities detected.
	22	AM	Dark faeces.
		PM	Dark faeces.
	23	AM	No abnormalities detected.
		PM	No abnormalities detected.
	24	AM	No abnormalities detected.
		PM	No abnormalities detected.
	25	AM	No abnormalities detected.
		PM	No abnormalities detected.
	26	AM	No abnormalities detected.
		PM	No abnormalities detected.
	27	AM	No abnormalities detected.
		PM	No abnormalities detected.
	28	AM	No abnormalities detected.
		PM	Quiet, huddled.
	29	AM	Quiet.
		PM	Alert and active.
	30	AM	Quiet but alert.
		PM	No abnormalities detected.
	31	AM	Quiet.
		PM	Alert and active.
	32	AM	Loose faeces.
		PM	Loose faeces.
	33	AM	Dark faeces.
		PM	Dark faeces.
	34	AM	Dark faeces.
		PM	Sacrificed.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W554f (continued)	1	AM	Quiet but alert.
		PM	Quiet but alert.
	2	AM	No abnormalities detected.
		PM	Quiet but alert. Crouched on perch.
	3	AM	Quiet and huddled.
		PM	Quiet and huddled.
	4	AM	Quiet but alert.
		PM	Quiet but alert.
	5	AM	Alert and active.
		PM	No abnormalities detected.
	6	AM	No abnormalities detected.
		PM	No abnormalities detected.
	7	AM	Quiet but alert. Dark faeces.
		PM	Quiet but alert. Dark faeces.
	8	AM	Dark faeces.
		PM	No faeces seen.
	9	AM	Dark faeces.
		PM	Quiet. Dark faeces.
	10	AM	Dark faeces.
		PM	Sacrificed.
W112f	1	AM	No abnormalities detected.
		PM	Quiet and huddled. No faeces seen.
	2	AM	No abnormalities detected.
		PM	Quiet but alert.
	3	AM	Quiet but alert.
		PM	Quiet but alert.
	4	AM	Quiet but alert.
		PM	Quiet but alert.
	5	AM	Quiet but alert.
		PM	Quiet and huddled.
	6	AM	Quiet but alert.
		PM	Quiet but alert.
	7	AM	Quiet and huddled.
		PM	Quiet.
	8	AM	Quiet. Dark faeces.
		PM	Quiet, huddled. Dark faeces. Reluctant to move. Sacrificed.
W741m	1	AM	Quiet.
		PM	Quiet. Huddled on cage floor.
	2	AM	Found dead.
W264f	1	AM	Quiet, huddled.
		PM	Quiet and huddled. Appears asleep.
	2	AM	Quiet, huddled. No reaction to stimulation.
		PM	Found dead

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W769m	1	AM	Alert and aggressive.
		PM	Quiet but alert.
	2	AM	Sacrificed.
W445m	1	AM	Quiet but alert. No faeces seen.
		PM	Quiet but alert.
	2	AM	Quiet but alert.
		PM	Quiet but alert.
	3	AM	Quiet but alert.
		PM	Quiet but alert.
	4	AM	Quiet but alert.
		PM	Quiet but alert.
	5	AM	Quiet but alert.
		PM	Alert and active.
	6	AM	Alert and active.
		PM	Quiet but alert.
	7	AM	Quiet but alert.
		PM	Alert and active.
	8	AM	Loose/liquid faeces.
		PM	No faeces seen.
	9	AM	Quiet but alert. Normal faeces.
		PM	Sacrificed.
W459m	1	AM	Quiet but alert. Reluctant to use legs.
		PM	Quiet but alert. Reluctant to use legs.
	2	AM	Quiet but alert.
		PM	Quiet but alert.
	3	AM	Quiet but alert.
		PM	Quiet but alert.
	4	AM	Quiet but alert.
		PM	Quiet but alert.
	5	AM	Quiet but alert.
		PM	Quiet but alert.
	6	AM	Alert and active.
		PM	Alert and active.
	7	AM	No abnormalities detected.
		PM	Dark faeces.
	8	AM	Alert and active. Dark faeces.
		PM	Sacrificed.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W450f	1	AM	Sacrificed.
W468f	1	AM	Alert and active.
		PM	Quiet but alert.
	2	AM	Quiet but alert.
		PM	Quiet but alert.
	3	AM	Alert and active.
		PM	Quiet but alert.
	4	AM	Alert and active.
		PM	Alert and active.
	5	AM	Alert and active.
		PM	Alert and active.
	6	AM	No abnormalities detected.
		PM	Dark faeces.
	7	AM	Alert and active. Dark faeces.
		PM	Alert and active. Dark faeces.
	8	AM	Quiet and huddled. Dark faeces.
		PM	Quiet and huddled. Dark faeces.
	9	AM	Quiet. Liquid faeces.
		PM	Quiet. Liquid faeces.
	10	AM	Quiet. Dark and loose faeces.
		PM	Quiet. Dark and loose faeces.
	11	AM	Quiet and huddled. Dark loose/liquid faeces.
		PM	Quiet and huddled. Dark loose/liquid faeces.
	12	AM	Quiet but alert. Pale liquid faeces.
		PM	Quiet but alert. Huddled. Pale liquid faeces.
	13	AM	Quiet and huddled. No loose faeces seen.
		PM	Quiet but alert.
	14	AM	Quiet and huddled.
		PM	Quiet but alert.
	15	AM	Quiet and huddled. Liquid faeces.
		PM	Quiet and huddled. No faeces seen.
	16	AM	Quiet but alert. Liquid faeces.
		PM	Quiet but alert. Liquid faeces.
	17	AM	Quiet but alert. Liquid faeces.
		PM	Quiet but alert. Liquid faeces.
	18	AM	Alert and active. Dark faeces.
		PM	Quiet and huddled.
	19	AM	Quiet and huddled. Loose faeces.
		PM	Alert and active.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W468f	20	AM	Quiet.
(continued)		PM	Tail amputated as gangrene increeping proximally.
	21	AM	Quiet but alert.
		PM	Quiet but alert.
	22	AM	Alert. Slightly unsteady.
		PM	Congested breathing.
	23	AM	Alert and active.
		PM	Quiet but alert.
	24	AM	Quiet but alert. Congested breathing.
		PM	Quiet but alert. Normal breathing.
	25	AM	Alert and active. Loose faeces.
		PM	Quiet but alert.
	26	AM	Sacrificed.
W467m	1	AM	Quiet and huddled.
		PM	Quiet and huddled.
	2	AM	Quiet but alert.
		PM	Quiet. Dark faeces.
	3	AM	Alert and active. Dark faeces.
		PM	Quiet but alert. Dark faeces.
	4	AM	Quiet. Piloerection. Dark faeces.
		PM	Quiet. Piloerection. Dark faeces.
	5	AM	Loose faeces.
		PM	Quiet but alert. Loose faeces.
	6	AM	Alert and active. Liquid faeces.
		PM	Alert and active. Liquid faeces.
	7	AM	Quiet but alert.
		PM	Quiet but alert.
	8	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	9	AM	Quiet but alert. No loose faeces seen.
		PM	Quiet but alert.
	10	AM	Quiet but alert.
		PM	Quiet but alert.
	11	AM	Quiet but alert.
		PM	Quiet but alert.
	12	AM	Quiet but alert.
		PM	Quiet but alert.
	13	AM	Quiet but alert.
		PM	Quiet but alert.
	14	AM	Quiet but alert.
		PM	Quiet but alert.
	15	AM	Quiet but alert.
		PM	Alert and active.
	16	AM	Quiet but alert.
		PM	Quiet but alert.
	17	AM	Quiet but alert.
		PM	Quiet but alert.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W467m (continued)	18	AM	Alert and active.
		PM	Quiet but alert.
	19	AM	Quiet. Dark faeces.
		PM	Sacrificed.
W747m	1	AM	Quiet.
		PM	Quiet.
	2	AM	Quiet but alert.
		PM	Dark faeces.
	3	AM	Alert and active. Dark faeces.
		PM	Quiet but alert. Dark faeces.
	4	AM	Piloerection. Dark faeces.
		PM	Alert and active.
	5	AM	Alert and active.
		PM	Quiet but alert.
	6	AM	Alert and active. Dark faeces.
		PM	Alert and active. Dark faeces.
	7	AM	Alert and active. Dark faeces.
		PM	Alert and active. Dark faeces.
	8	AM	Alert and active. Dark faeces.
		PM	Alert and active. Dark faeces.
	9	AM	Quiet but alert. No loose faeces seen.
		PM	Quiet but alert.
	10	AM	Quiet but alert.
		PM	Quiet but alert.
	11	AM	Quiet but alert.
		PM	Alert and active.
	12	AM	Alert and active.
		PM	Alert and active.
	13	AM	Quiet but alert.
		PM	Quiet.
	14	AM	Quiet but alert.
		PM	Quiet but alert.
	15	AM	Quiet but alert.
		PM	Quiet but alert.
	16	AM	Quiet but alert.
		PM	Quiet but alert.
	17	AM	Quiet but alert.
		PM	Quiet but alert.
	18	AM	Quiet but alert.
		PM	Quiet but alert.
	19	AM	No abnormalities detected.
		PM	Quiet.
	20	AM	Quiet but alert.
		PM	Quiet but alert.
	21	AM	Quiet but alert.
		PM	Quiet but alert.
	22	AM	Quiet but alert.
		PM	Quiet but alert. Animal found dead. No discharge from nose or mouth. No sign of any vomit. Rigor mortis set in.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W763m	1	AM	Quiet but alert and awake.
		PM	Asleep on perch, later quiet but alert.
	2	AM	Alert and active.
		PM	Alert and active.
	3	AM	Quiet but alert.
		PM	Quiet but alert.
	4	AM	Alert and active.
		PM	Alert and active.
	5	AM	Alert and active. Blood in tray.
		PM	Alert and active. Blood in tray.
	6	AM	Alert and active.
		PM	Quiet but alert.
	7	AM	Alert and active.
		PM	Alert and active.
	8	AM	Alert and active.
		PM	Alert and active.
	9	AM	Alert and active.
		PM	Quiet but alert.
	10	AM	Quiet but alert.
		PM	Alert and active.
	11	AM	Alert and active.
		PM	Quiet but alert.
	12	AM	Quiet but alert.
		PM	Quiet but alert.
	13	AM	Quiet but alert.
		PM	Quiet but alert.
	14	AM	Quiet but alert.
		PM	Quiet and huddled but alert.
	15	AM	Quiet but alert.
		PM	Quiet but alert.
	16	AM	Quiet but alert.
		PM	Quiet but alert.
	17	AM	Quiet but alert. Liquid faeces
		PM	Quiet but alert.
	18	AM	Quiet but alert. Liquid faeces.
		PM	Quiet but alert. Normal faeces.
	19	AM	Quiet but alert.
		PM	Quiet but alert.
	20	AM	Quiet but alert.
		PM	Quiet but alert.
	21	AM	Quiet but alert.
		PM	Quiet. Huddled.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day		Clinical signs
W763m (continued)	22	AM	Quiet. Huddled. Loose faeces.
		PM	Quiet. Huddled. Loose faeces.
	23	AM	Quiet but alert. Loose faeces.
		PM	Quiet but alert. Loose faeces.
	24	AM	Quiet and huddled. Swelling around both eyes. Loose faeces. Oedema on abdomen.
		PM	Quiet and huddled. Swelling around both eyes. Loose faeces. Oedema on abdomen.
	25	AM	Quiet but alert, occasionally huddled. Loose faeces. Swelling around both eyes. Oedema on abdomen.
		PM	Quiet but alert, occasionally huddled. Loose faeces. Swelling around both eyes. Oedema on abdomen.
	26	AM	Quiet but alert, occasionally huddled. Swelling around both eyes.
		PM	Quiet but alert. Huddled. Swelling around both eyes.
	27	AM	Quiet but alert. Swelling around both eyes. Normal faeces.
		PM	Quiet but alert. Swelling around both eyes.
	28	AM	Quiet and huddled. Swelling around both eyes.
		PM	Very quiet and huddled. Swelling around both eyes.
	29	AM	Quiet. Reluctant to move. Increased swelling around eyes.
		PM	Sacrificed.
W13m	1	AM	Quiet and huddled. Appears asleep.
		PM	Quiet and huddled. Appears tired.
	2	AM	Quiet but alert. Huddled.
		PM	Quiet but alert. Huddled.
	3	AM	Quiet but alert.
		PM	Quiet but alert.
	4	AM	Quiet but alert.
		PM	Quiet but alert.
	5	AM	Quiet but alert.
		PM	Quiet but alert.
	6	AM	Quiet but alert.
		PM	Quiet but alert.
	7	AM	Quiet but alert.
		PM	Quiet but alert.
	8	AM	Quiet.
		PM	Quiet, huddled. Loose faeces.
	9	AM	Quiet, huddled. Loose faeces.
		PM	Sacrificed.

APPENDIX 9

Clinical signs

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported for the day of transplant (Day 0). No animals survived beyond Day 0.

Animal no./sex	Day	Clinical signs
W26f	0 am	Quiet but alert. No other abnormalities recorded.
	0 pm	No palpable beat from transplanted heart. Possible rejection. Sacrificed.
W44f	0 am	No abnormalities detected. Heart not viable. Sacrificed under anaesthesia in theatre
W28f	0 am	Vomit in cage. No other abnormalities detected.
	0 pm	Sacrificed.
W4f	0 am	Vomit in cage. No other abnormalities detected. Sacrificed under anaesthesia in theatre. Heart stopped. Sacrificed under anaesthesia in theatre.

EXPERIMENTAL PROCEDURE

ANIMAL SUPPLY

Donor animals

Transgenic piglets were selected from litters produced by the Sponsor under Project Licence No. PPL [redacted] Transgenic piglets supplied for the study were >21 days old.

Recipient animals

Captive-bred cynomolgus monkeys (*Macaca fascicularis*) were selected from shipments of animals bred at [redacted] They were imported through a UK commercial supplier [redacted] The age of the animals at allocation to the study was 1½ - 3¼ years and their weights were in the range 1.9 to 3.5 kg.

Initially a group of 10 – 12 animals was allocated to the study for screening as suitable recipients. Of these, 8 animals were selected by the Sponsor for transplant. Animals of both sexes were allocated, although there was no scientific requirement to maintain a balanced sex-ratio. Additional animals were screened in order to select further suitable recipients.

ANIMAL MANAGEMENT

All animals were conditioned in England for at least 4 weeks before delivery to the Huntingdon Life Research Centre. Documentation received from the supplier included details relating to quarantine dates, health screening and any treatment administered during the conditioning period. On arrival at HRC they were examined by a Veterinary Officer and allocated a unique colony number, which was tattooed under the right arm. Intrapalpebral tuberculin tests were performed at intervals of approximately 6 weeks, beginning soon after arrival. For transplanted animals, due to the frequency of planned laboratory investigations and due to the nature of the study, intrapalpebral tuberculin testing was stopped following transplant.

The animals were housed initially individually and later in pairs in cages specifically designed to house non-human primates in clean and secure conditions. The animals were housed in cages measuring 78 cm wide, 103 cm deep and 230 cm high. The cages were constructed of a stainless steel framework and printboard walls, shelves and ceiling, incorporating a squeeze-back system, food hopper, water bottle holder and a removable 2.5 × 2.5 cm grid floor. Under the front half of each cage was a removable tray which contained wood chippings (Gold Chips sawdust: [redacted] for use as a litter/forage substrate. The cages were cleaned and litter replaced each day after recording any food residues. Automatic drinking valves, for the supply of drinking water, were used and were fitted in both upper and lower parts of the cage.

The rooms in which the animals were kept were as far as practicable isolated from external disturbances. The room temperature was maintained within the range 19 to 25°C, using heat exchangers connected to hot water supplied from oil-fuelled boilers. Relative humidity was maintained within the range 36 to 84%. The environment was governed by a computer controlled building management system which continuously monitored the temperature and humidity controls and the operational state of the air handling plant. Temperature and relative humidity were recorded using a Rototherm Recorder. Deviations in temperature and/or relative humidity outside the set limits (20 - 26°C, 45 – 70% RH) were generally due to the use of fan heaters as supplementary heat sources and when water was used to wash down cages and/or floors. Artificial lighting was used and was controlled to give 12 hours of light and 12 hours of dark per 24 hours. Air extraction was via a balanced system designed to give fifteen air changes per hour.

FOOD AND WATER

Cynomolgus monkeys were each offered 200 or 150 grams, of standard dry diet ([redacted]), daily, usually in the morning. In the morning, the residue of the previous day was removed and weighed. All animals were starved overnight prior to operation.

Water was available at all times, except when specifically withheld during urine collection for Phase IV and V animals. Vitamin C (Blackcurrant, [redacted]) and [redacted] (a vitamin B_{12} preparation, [redacted]) were added to the drinking water on one day of each week.

There was no information available to the Study Director to indicate that any non-nutrient substance likely to influence the effect of the test substance could reasonably be expected to be present in the diet or the drinking water, both of which were routinely subjected to chemical analysis. Results of all the analyses were lodged in the Huntingdon Life Sciences Archives.

Wholemeal bread and fresh fruit or vegetable produce were offered in order to enrich the environment and improve the interaction between the animals and their handlers.

STUDY DESIGN

Groups of animals received transplants of islets cultured from either transgenic (hDAF+ve) or control (hDAF-ve) foetal pig pancreas.

The study design is as summarised overleaf.

Phase	Group	hDAF Expression	Immunosuppressive Treatment	Animal numbers
I	1	+	No	W540f W566f
II	2	-	No	W546f W550f
	3	+	Yes	W627m W610f W628f W622f
	4	-	Yes	W621f
	5	+	No#	W546f
III	6	+	Yes	W397m W298m
	7	-	Yes	W421m W417m W433m W542f
IV	8	-	Yes	W419m W615m
	9	+	Yes	W742f W634f W612f W607m*
V	10	+	Yes	W773m W746f W766f
VI	11	+	Yes	X34f X36f X51m X52f
	12	-	Yes	X40f W757m W759m W760f
	13	+	Yes	W458f W750f W762f W774f

\# Received a single dose [redacted] of [redacted] on the day of transplant (Day 0)

* Received transplant of islet under the capsule of the left kidney only – all other animals on this phase received transplants as an omental sac also

All animals that underwent transplant received immunosuppressive treatment with a combination of [redacted] immunosuppressive treatment commenced on [redacted] the day of transplant being designated Day 0.

Details of recipients for transplants and the dates they were performed on are listed in Appendix 1. All recipient animals were identified by their unique HLS colony number.

The study was designed such that all animals initially followed a standard immunosuppressive protocol prior to and immediately following transplant. After a few days the immunosuppressive regime was then individually tailored for each animal being based on the results of laboratory investigations and blood drug levels. The initial dosing regimes are summarised as follows:

[redacted] was initially administered as [redacted] administered by intramuscular injection on Days [redacted] at a dosage level of [redacted]. Oral administration of [redacted] commenced on Day [redacted] at a dosage level advised by the Sponsor and was given by gavage as a split dose morning and late afternoon.

[redacted] was administered by intravenous injection on Day [redacted] at a dosage level of [redacted] and on Day [redacted] at [redacted] Administration was continued from Day [redacted] at a dosage of [redacted] and was administered orally.

[redacted] was administered by intravenous injection at a dosage level of [redacted] at the time of transplant. Animals were dosed orally with [redacted] at the same dosage level on Days [redacted] and [redacted] after which the dosage level was reduced daily by [redacted] increments until a dosage of [redacted] was reached. Thereafter animals were maintained at that dosage level until advised otherwise by the Sponsor.

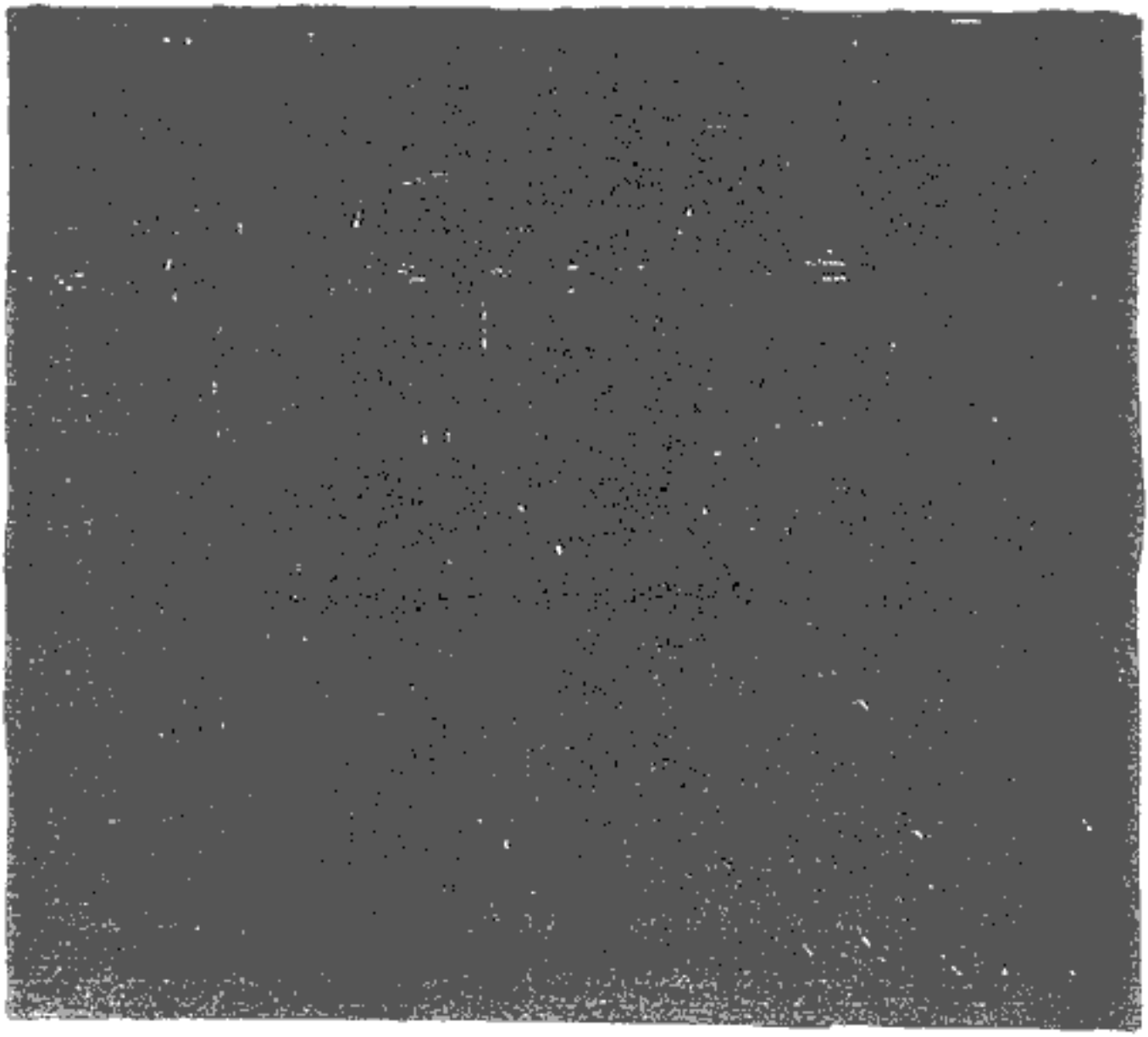
[redacted] was administered orally by gavage on Day [redacted] at a dosage of [redacted] and subsequently on alternate days (Day 1, 3, 5 *etc*) at a dosage of [redacted]

Details of the immunosuppressive regimes applied to individual animals are presented in Appendix 3.

Transplant operations were performed on various numbers of recipient animals per day and were spread over a period of 10 weeks, dependent on the availability of suitable donor animals. The commencement of the study for these subgroups was therefore varied dependent on when the transplant was performed.

The animals were housed in the [redacted]

PREPARATION OF THE IMMUNOSUPPRESSANT TREATMENTS



ADMINISTRATION OF THE IMMUNOSUPPRESSANT TREATMENTS

The animals were dosed at approximately the same time each morning, late afternoon and evening when applicable. Individual doses were adjusted daily according to the most recent bodyweight. The required quantity of each test solution was measured into a suitably graduated plastic syringe.

For oral dosing the test solutions were administered through a plastic catheter [redacted] inserted via the mouth into the stomach. The catheter was flushed through with 10 ml of a high carbohydrate, low electrolyte, low fluid drink; [redacted]

For intravenous administration, the test solution was injected using a [redacted] infusion set inserted into the cephalic or saphenous vein.

For intramuscular administration, the test solution was injected through an appropriate gauge hypodermic needle. The animal was dosed in the thigh, the hair having been removed by clipping to facilitate administration and to observe any local reaction to the injection.

Intravenous administration of steroid on the day of transplant was carried out during surgery. The dose was administered through an indwelling cannula inserted into a peripheral vein.

PRE-OPERATIVE INVESTIGATIONS

During the acclimatisation period, blood samples were obtained from potential recipient animals for various investigations. Whole blood samples were obtained for the following investigations.

1. 10 ml into plain tubes

   - Anti-pig antibody titres
   - CH50
   - Blood group
   - C-peptide assay

2. 200 µl into Alsevers solution

   - Flow cytometry for T & B lymphocyte subsets

Following collection, the blood samples were immediately transported to [redacted] for analysis.

On the day of transplant, a whole blood sample (1 ml) was taken into a plain tube. A 200 µl aliquot was transferred to a tube containing Alservers solution for flow cytometry analysis. The remainder was used for C-peptide assay. On each occasion the samples were despatched on ice to [redacted] for investigations.

SURGICAL PROCEDURE

Recipient animals

All animals were starved overnight prior to surgery. Prior to transfer to the operating theatre the animal was sedated with [redacted] given by the intramuscular route in combination with [redacted].

Following induction of anaesthesia by intravenous injection of [redacted] an endotracheal tube was inserted and the animals were maintained on a [redacted] mixture, with the addition of [redacted] at a concentration of [redacted] as required.

Prophylactic antibiotic therapy [redacted], was given by intramuscular injection.

An indwelling cannula was inserted into a peripheral vein for administration of fluids and drugs *etc* during the procedure. The animal was transferred to the operating table where appropriate respiratory and electrocardiographic monitoring was established.

The abdominal skin was then prepared with aqueous based betaine solution and sterile drapes applied to expose the operative field. The abdomen was opened via a midline or paracostal incision from slightly above the symphysis pubis to the mid-epidastrium. The wound was held open with a self-retaining retractor.

The bowel was packed into the right hand side of the abdomen using a damp swab and malleable lead retractor. The left kidney was visualised and a small opening made in the renal capsule at the posterior pole. A metal probe was introduced into the opening to make a tunnel by separating the capsule from the underlying renal cortex. A purse-string suture was made around the opening.

The pancreas fragments, prepared and supplied by the Sponsor, were placed in a 5 ml plastic syringe with 16G plastic tubing attached. The plastic tubing was inserted into the pocket and the pancreas pieces extruded as the tube was withdrawn. The opening to the pocket was closed by tying the suture.

The intention was to infiltrate approximately 50 – 100 pancreas pieces over a tract of approximately 2 cm, which would subsequently be clearly visible through the kidney capsule.

The bowel was then repositioned and the abdomen closed with a single layer of loop nylon to the linea alba, 2:0 vicryl to the subcutaneous tissues and the skin closed with subcuticular vicryl. Antiseptic spray was then applied to the wound.

The animal was allowed to recover from anaesthesia before being returned to the animal room. During this time a small blood sample was obtained by needle stab of the thumb, for the measurement of blood glucose using a proprietary test strip (stick).

Organ-cultured pancreas for transplant

Organ-cultured foetal pancreas tissue from transgenic (hDAF+ve) and control (hDAF-ve) pigs were brought to HRC by the Sponsor on the morning of the transplant.

POST-OPERATIVE MANAGEMENT

Recipient animals were closely monitored until fully recovered from the operation.

Post-operative analgesia was provided by the use of [redacted], which was administered at the discretion of the attending veterinary surgeon. Other drugs were prescribed if considered appropriate. Details of individual drug administrations were recorded in the study records.

Animals received a single administration of [redacted] solution) on the day prior to transplant. From Day 1, one or two doses were given daily at the discretion of the attending veterinarian. Animals received a subcutaneous dosage of [redacted]

The animals were observed at regular intervals during the working day and their condition reviewed as necessary with the Sponsor's Monitoring Scientist or Veterinarian.

Animals receiving immunosuppressant treatment were given [redacted] orally, twice daily at a dosage of [redacted]

In the case of repeated or marked inappetance, food and/or fluid (oral and/or intravenous) supplements were given at the discretion of the attending veterinary surgeon and/or Sponsor's Monitoring Scientist.

POST-OPERATIVE OBSERVATIONS

Dated and signed records of all activities relating to the day by day running and maintenance of the study within the animal unit, as well as to the group observations and examinations outlined in this protocol, were recorded in the Study Day Book. In addition, observations relating to individual animals made throughout the day were recorded.

The following observations were made during the course of the study:

Clinical signs

All signs of ill health or reaction to treatment were recorded. Animals were checked regularly throughout the working day from approximately 0800 to 1700 hours (including weekends and public holidays). The animals were removed from their cages at least twice a day to assess their general condition (see POST-OPERATIVE INVESTIGATIONS).

Bodyweight

The bodyweight of all animals was recorded at approximately weekly during the pre-dose period and daily from Day 0 (Phase I) or Day –1 (Phase II onwards). The animals were weighed in the morning prior to dosing or at a similar time during the predose period.

Food consumption

The quantity of food (standard dry diet) left by each animal or pair of animals together with an estimate of the quantity spilled was recorded on a daily basis throughout the experimental period.

POST-OPERATIVE INVESTIGATIONS

Animals were removed from their cages each morning and afternoon to check their general physical condition and for the administration of immunosuppressant and/or other treatments as required.

Blood sampling

Blood samples were obtained for each phase of the study as follows:

Phase I

Haematology	Monday, Wednesday and Friday
Biochemistry	Monday, Wednesday and Friday
Antibodies/C-peptide	Every weekday
Flow cytometry	No samples required
[redacted]	No samples required

Phase II

Haematology	Monday, Wednesday and Friday
Biochemistry	Monday, Wednesday and Friday
Antibodies/C-peptide	Monday, Wednesday and Friday
[redacted]	Monday, Wednesday and Friday
Flow cytometry	Once weekly

Phases III, IV and V

Haematology	Monday, Wednesday and Friday
Biochemistry	Monday, Wednesday and Friday
Antibodies/C-peptide	Monday, Wednesday and Friday
[redacted]	Monday, Wednesday and Friday

Phase VI

Haematology	Monday, Wednesday and Friday
Biochemistry	Monday, Wednesday and Friday
Antibodies/C-peptide	Monday, Wednesday and Friday
[redacted]	Monday, Wednesday and Friday
	Each weekday

The 0.5 ml blood samples for measurement of [redacted] were collected into plain microtainer tubes and were sent to [redacted] for analysis.

Blood samples were taken in the morning and for Phase II – VI prior to any dosing if scheduled. The frequency of the investigations were sometimes altered for individual animals, on the recommendation of the Sponsor's Monitoring Scientist or HRC veterinarian and were documented in the Study Daybook.

The type of blood samples and the investigations performed were as follows:

(a) **Laboratory investigations performed at Huntingdon Life Sciences**

The results of the haematology and biochemistry investigations detailed below were notified by fax to [redacted] or [redacted] as soon as they became available.

Haematology	Units
300 µl into 0.5 ml EDTA tube. The following investigations were performed using a Bayer-Technicon H1E haematology analyser	
Packed cell volume (PCV)	%
Haemoglobin (Hb)	g/dl
Red blood cell count (RBC)	$\times 10^{12}/l$
Total white cell count (WBC Total)	$\times 10^{9}/l$
Platelet count (Plts)	$\times 10^{9}/l$
Differential WBC count	
Neutrophils (N))	
Lymphocytes (L))	
Eosinophils (E))	$\times 10^{9}/l$
Basophils (B))	
Monocytes (M))	

Cell Morphology : the most common morphological changes (anisocytosis, micro/macrocytosis, variation in colour, hypo/hyperchromasia, left shift, atypical/blast cells) were recorded as follows:

- \- = No abnormalities detected
- \+ = slight
- ++ = moderate
- +++ = marked

In the case of atypical/blast cells, or other abnormalities, confirmation or a written description from a blood film was made.

Biochemistry	Units
700 µl into heparinised microtainer. The following parameters were analysed with a Hitachi 737 Clinical Chemistry analyser	
Urea (Urea)	mg/dl
Creatinine (Creat)	mg/dl
Sodium (Na)	mEq/l
Potassium (K)	mEq/l
Calcium (Ca)	mEq/l
Inorganic Phosphorus (P)	mEq/l
Chloride (Cl)	mEq/l
Osmolality (Osmo) - using a Wescor vapour-pressure osmometer	mOsm/kg
Total protein (Total Prot)	g/dl
Albumin (Alb)	g/dl
Globulin (Glob) : by subtraction Total protein (g/dl) minus Albumin (g/dl)	g/dl

(b) **Blood samples for despatch to** [redacted] or [redacted]

Anti-pig antibody levels and C-peptide assay (Serum)

1.0 ml into a plain tube. Samples were analysed at [redacted]

Flow cytometry (Alservers)

200 µl into tubes containing Alservers solution (supplied by the Sponsor). Samples were analysed at [redacted]

[redacted]

0.2 ml into 0.5 ml EDTA tube. Samples were analysed at [redacted]

(c) **Urine samples for despatch to** [redacted]

Prior to termination of Phase IV and Phase V animals, overnight collection of urine was performed on two occasions. Prior to the start of collection (approximately 1700), water was withdrawn from the animals. Urine was collected overnight until approximately 0900 the next morning. A small aliquot (ca 20 ml) of the urine sample was taken and deep frozen incardice prior to despatch to [redacted] for analysis.

Biopsy of pancreatic islet grafts

Biopsies of the pancreatic islet graft sites were performed as follows:

Phase I	biopsied on Day 3
Phase II	biopsied on Day 14
Phase III	biopsied on Day 27
Phase IV	biopsied on Day 35 with the exception of animal W607m biopsied on Day 34
Phase V	biopsied on Day 30 (W746f and W766f) and Day 37 (W773m)
Phase VI	biopsied on Day 14 (Groups 12 and 13) and Day 28 (Group 11)

Under general anaesthesia a small incision was made in the abdomen. The graft site was biopsied by a small superficial wedge incision in the graft, after opening the kidney capsule. Haemostasis was achieved by cautery and the incision reclosed over a small piece of gelatin foam to achieve tamponade. The biopsy specimen was placed in Bouin's fixative prior to despatch to the Sponsor for examination.

TERMINAL STUDIES

Pre-terminal blood sampling

Prior to sacrifice as much blood as practicable was collected and divided appropriately into heparinised and plain blood tubes.

Following centrifugation the plasma/serum was separated and stored deep frozen (in cardice) prior to despatch to the Sponsor for analysis.

Necropsy procedure

Each animal was immobilised with [redacted] given by the intramuscular route. The animals were then killed by a lethal dose of [redacted] and then rapidly exsanguinated by incision of the carotid blood vessels.

The left kidney with its capsule still intact was removed. The graft site was biopsied and the specimen placed in Bouin's fixative. A further small piece of kidney was taken for virus studies (see below). The remainder of the kidney was placed in neutral buffered formalin.

Virus studies

Samples of the following tissues were required to be taken from all recipient animals where the xenograft had survived in excess of 5 days. The size of the sample was ideally approximately 0.5 cm^3 or if this size was not possible, as much was feasible.

- renal capsule that has been in contact with the transplanted islets
- heart
- lung
- liver
- ovaries or testes
- pancreas
- brain
- ileum
- mid-colon

For Phase V and VI animals, in addition to the samples listed above, addition samples of spleen were taken from all animals at *post mortem* as follows:

- two pieces were collected into cryovials and frozen in liquid nitrogen
- two pieces were placed on cork discs, covered in OCT-embedding matrix and rapidly frozen in liquid nitrogen. Each piece was wrapped in foil

All samples were snap frozen in liquid nitrogen and stored deep frozen (ca -70°C) prior to despatch to, or collection by the Sponsor.

LOCATION OF STUDY RECORDS

All specimens (except those sent to the Sponsor or other third party), raw data and other documents generated at Huntingdon Life Sciences, together with a copy of the final report were lodged in the Huntingdon Life Sciences Archives, Huntingdon, England.

Such specimens and records were retained for a minimum period of five years from the date of issue of the final report. At the end of the five year retention period the Client will be contacted and advice sought on their future requirements. Under no circumstances will any item be discarded without the Client's knowledge.

Data arising from any investigations made by the Sponsor or other third party, the findings of which are included in the Huntingdon Life Sciences final report, was retained and archived by the Sponsor.

PROCEDURES

The procedures used during the study were documented in the relevant Huntingdon Life Sciences Procedures Manual.

APPENDIX 8

Individual clinical signs

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1).

APPENDIX 8

(Clinical signs – continued)

Phase	Animal no./sex	Day		Clinical signs
I	W540f	1	am	Quiet but alert.
			pm	Quiet but alert.
		2	am	Quiet but alert.
			pm	Quiet but alert.
		3	am	Quiet but alert.
			pm	Quiet. 22.30 Alert and active, picking at stitches.
		4	am	Quiet but alert.
			pm	Quiet but alert.
		5	am	Quiet but alert.
			pm	Quiet but alert.
		6	am	Quiet but alert.
			pm	Alert and active.
		7	am	Alert and active, loose faeces.
			pm	Sacrificed.
	W564f	1	am	Quiet but alert.
			pm	Quiet but alert.
		2	am	Quiet but alert.
			pm	Quiet but alert.
		3	am	Quiet but alert.
			pm	Quiet. 22.30 Alert and active.
		4	am	Quiet but alert.
			pm	Quiet but alert.
		5	am	Quiet but alert.
			pm	Quiet but alert.
		6	am	Quiet but alert.
			pm	Alert and active.
		7	am	Alert and active.
			pm	Sacrificed.
	W566f	1	am	Quiet but alert.
			pm	Quiet but alert.
		2	am	Quiet but alert.
			pm	Quiet but alert.
		3	am	Quiet but alert.
			pm	Quiet. 22.30 Alert and active.
		4	am	Quiet but alert.
			pm	Quiet but alert.
		5	am	Quiet but alert.
			pm	Quiet but alert.
		6	am	Quiet but alert.
			pm	Alert and active.
		7	am	Alert and active.
			pm	Sacrificed.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day no.		Clinical signs
I (cont)	W550f	1	am	Quiet but alert.
			pm	Quiet but alert.
		2	am	Quiet but alert.
			pm	Quiet but alert.
		3	am	Quiet but alert.
			pm	Quiet. 22.30 Alert and active.
		4	am	Quiet but alert.
			pm	Quiet but alert.
		5	am	Quiet but alert.
			pm	Quiet but alert.
		6	am	Quiet but alert.
			pm	Alert and active.
		7	am	Alert and active.
			pm	Sacrificed.
II	W610f	1	am	Alert and active. Vomit in cage.
			pm	Quiet but alert.
		2	am	Quiet but alert.
			pm	Quiet but alert.
		3	am	Quiet but alert.
			pm	Quiet but alert.
		4	am	Quiet but alert.
			pm	Quiet but alert.
		5	am	Quiet but alert.
			pm	Quiet but alert.
		6	am	Quiet but alert.
			pm	Quiet but alert.
		7	am	Quiet but alert.
			pm	Quiet but alert.
		8	am	Quiet but alert.
			pm	No abnormalities detected.
		9	am	No abnormalities detected.
			pm	No abnormalities detected.
		10	am	No abnormalities detected.
			pm	No abnormalities detected.
		11	am	No abnormalities detected.
			pm	No abnormalities detected.
		12	am	No abnormalities detected.
			pm	No abnormalities detected.
		13	am	No abnormalities detected.
			pm	No abnormalities detected.
		14	am	Recovering from sedation.
			pm	No abnormalities detected.
		15	am	No abnormalities detected.
			pm	No abnormalities detected.
		16	am	Quiet but alert.
			pm	Quiet but alert.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
II (cont)	W610f (cont)	17	am	Quiet but alert, loose faeces.
			pm	Quiet but alert, loose faeces.
		18	am	Quiet but alert, loose faeces.
			pm	Quiet but alert, loose faeces.
		19	am	Quiet but alert.
			pm	No abnormalities detected.
		20	am	Quiet but alert.
			pm	Quiet but alert.
		21	am	No abnormalities detected.
			pm	No abnormalities detected.
		22	am	No abnormalities detected.
			pm	No abnormalities detected.
		23	am	Quiet but alert.
			pm	Quiet but alert.
		24	am	Quiet.
			pm	Quiet.
		25	am	Quiet.
			pm	No abnormalities detected.
		26	am	Quiet.
			pm	Quiet and huddled.
		27	am	Quiet.
			pm	Quiet.
		28	am	Quiet but alert.
			pm	Quiet but alert. Sacrificed.
	W627m	1	am	Quiet but alert.
			pm	Quiet but alert.
		2	am	Quiet but alert.
			pm	Quiet but alert.
		3	am	Quiet but alert.
			pm	Quiet but alert.
		4	am	Quiet but alert. Loose pale faeces.
			pm	Quiet but alert.
		5	am	Quiet but alert.
			pm	Quiet but alert.
		6	am	Quiet but alert.
			pm	Quiet but alert.
		7	am	Quiet but alert.
			pm	Quiet but alert.
		8	am	Alert and active.
			pm	No abnormalities detected.
		9	am	No abnormalities detected.
			pm	No abnormalities detected.
		10	am	No abnormalities detected.
			pm	No abnormalities detected.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
II (cont)	W627m (cont)	11	am	No abnormalities detected.
			pm	No abnormalities detected.
		12	am	No abnormalities detected.
			pm	No abnormalities detected.
		13	am	No abnormalities detected.
			pm	No abnormalities detected.
		14	am	No abnormalities detected.
			pm	Recovering from sedation.
		15	am	No abnormalities detected.
			pm	No abnormalities detected.
		16	am	Quiet but alert.
			pm	Quiet but alert.
		17	am	Quiet but alert.
			pm	Quiet but alert.
		18	am	Quiet but alert.
			pm	No abnormalities detected.
		19	am	No abnormalities detected.
			pm	No abnormalities detected.
		20	am	Quiet but alert.
			pm	Quiet but alert.
		21	am	No abnormalities detected.
			pm	No abnormalities detected.
		22	am	No abnormalities detected.
			pm	No abnormalities detected.
		23	am	Quiet but alert.
			pm	Quiet but alert.
		24	am	Quiet.
			pm	Quiet.
		25	am	Quiet.
			pm	No abnormalities detected.
		26	am	Clear nasal discharge.
			pm	Quiet and huddled.
		27	am	Quiet.
			pm	Quiet.
		28	am	Quiet but alert.
			pm	Quiet but alert. Sacrificed.
	W621m	1	am	Quiet but alert.
			pm	Quiet but alert.
		2	am	Quiet but alert.
			pm	Quiet but alert.
		3	am	Quiet but alert.
			pm	Quiet but alert.
		4	am	Quiet but alert.
			pm	Quiet but alert.
		5	am	Quiet but alert.
			pm	Quiet but alert.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
II (cont)	W627m (cont)	6	am	Quiet but alert. Sneezing.
			pm	Quiet but alert.
		7	am	Alert and active.
			pm	No abnormalities detected.
		8	am	No abnormalities detected.
			pm	No abnormalities detected.
		9	am	No abnormalities detected.
			pm	No abnormalities detected.
		10	am	No abnormalities detected.
			pm	No abnormalities detected.
		11	am	No abnormalities detected.
			pm	No abnormalities detected.
		12	am	No abnormalities detected.
			pm	No abnormalities detected.
		13	am	No abnormalities detected.
			pm	Recovering from sedation.
		14	am	No abnormalities detected.
			pm	No abnormalities detected.
		15	am	Quiet but alert.
			pm	Quiet but alert.
		16	am	Quiet but alert.
			pm	Quiet but alert.
		17	am	Quiet but alert.
			pm	Quiet but alert.
		18	am	No abnormalities detected.
			pm	No abnormalities detected.
		19	am	No abnormalities detected.
			pm	Alert and active.
		20	am	Loose faeces.
			pm	Loose faeces.
		21	am	No abnormalities detected.
			pm	No abnormalities detected.
		22	am	No abnormalities detected.
			pm	Quiet and huddled.
		23	am	Quiet.
			pm	Quiet.
		24	am	Quiet.
			pm	Quiet.
		25	am	Quiet.
			pm	Quiet and huddled.
		26	am	Sneezing.
			pm	Quiet and huddled.
		27	am	Quiet and huddled.
			pm	Quiet.
		28	am	Quiet.
			pm	Sacrificed.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
II (cont)	W628f	1	am	Quiet but alert.
			pm	Quiet but alert.
		2	am	Quiet but alert.
			pm	Quiet but alert.
		3	am	Quiet but alert.
			pm	Quiet but alert.
		4	am	Quiet but alert.
			pm	Quiet but alert.
		5	am	Quiet but alert.
			pm	Quiet but alert.
		6	am	Quiet but alert.
			pm	Quiet but alert.
		7	am	Alert and active. Loose faeces.
			pm	No abnormalities detected.
		8	am	No abnormalities detected.
			pm	No abnormalities detected.
		9	am	No abnormalities detected.
			pm	No abnormalities detected.
		10	am	No abnormalities detected.
			pm	No abnormalities detected.
		11	am	No abnormalities detected.
			pm	No abnormalities detected.
		12	am	No abnormalities detected.
			pm	No abnormalities detected.
		13	am	No abnormalities detected.
			pm	Recovering from sedation.
		14	am	No abnormalities detected.
			pm	No abnormalities detected.
		15	am	Quiet but alert.
			pm	Quiet but alert.
		16	am	Quiet but alert.
			pm	Quiet but alert.
		17	am	Quiet but alert.
			pm	No abnormalities detected.
		18	am	No abnormalities detected.
			pm	No abnormalities detected.
		19	am	No abnormalities detected.
			pm	Alert and active.
		20	am	No abnormalities detected.
			pm	No abnormalities detected.
		21	am	Sneezing.
			pm	No abnormalities detected.
		22	am	Sneezing.
			pm	No abnormalities detected.
		23	am	Quiet.
			pm	Quiet.
		24	am	No abnormalities detected.
			pm	No abnormalities detected.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
II (cont)	W628f (cont)	25	am	Quiet.
			pm	Quiet.
		26	am	No abnormalities detected.
			pm	No abnormalities detected.
		27	am	Quiet and huddled.
			pm	Quiet.
		28	am	Quiet.
			pm	Sacrificed.
	W622f	1	am	Quiet but alert.
			pm	Quiet but alert.
		2	am	Quiet but alert.
			pm	Quiet but alert.
		3	am	Quiet but alert.
			pm	Quiet but alert.
		4	am	Quiet but alert.
			pm	Quiet but alert.
		5	am	Quiet but alert.
			pm	Quiet but alert.
		6	am	Alert and active.
			pm	No abnormalities detected.
		7	am	No abnormalities detected.
			pm	No abnormalities detected.
		8	am	No abnormalities detected.
			pm	No abnormalities detected.
		9	am	No abnormalities detected.
			pm	No abnormalities detected.
		10	am	No abnormalities detected.
			pm	No abnormalities detected.
		11	am	No abnormalities detected.
			pm	No abnormalities detected.
		12	am	No abnormalities detected.
			pm	Recovering from sedation.
		13	am	No abnormalities detected.
			pm	No abnormalities detected.
		14	am	Quiet but alert.
			pm	Quiet but alert.
		15	am	Quiet but alert.
			pm	Quiet but alert.
		16	am	Quiet but alert.
			pm	Quiet but alert.
		17	am	No abnormalities detected.
			pm	No abnormalities detected.
		18	am	No abnormalities detected.
			pm	No abnormalities detected.
		19	am	No abnormalities detected.
			pm	No abnormalities detected.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
II (cont)	W622f (cont)	20	am	No abnormalities detected.
			pm	No abnormalities detected.
		21	am	No abnormalities detected.
			pm	No abnormalities detected.
		22	am	No abnormalities detected.
			pm	No abnormalities detected.
		23	am	No abnormalities detected.
			pm	No abnormalities detected.
		24	am	Quiet.
			pm	Quiet.
		25	am	No abnormalities detected.
			pm	Quiet.
		26	am	No abnormalities detected.
			pm	No abnormalities detected.
		27	am	No abnormalities detected.
			pm	No abnormalities detected.
		28	am	No abnormalities detected.
			pm	Sacrificed.
	W546f	1	am	Quiet, congested breathing.
			pm	Quiet, congested breathing.
		2	am	Quiet but alert, congested breathing.
			pm	Quiet but alert, congested breathing.
		3	am	Quiet but alert, congested breathing.
			pm	Quiet but alert, congested breathing.
		4	am	Quiet but alert, breathing improved.
			pm	Quiet but alert, breathing improved.
		5	am	Quiet but alert, breathing improved.
			pm	Quiet but alert, breathing improved.
		6	am	Alert and active. Breathing normal.
			pm	Alert and active.
		7	am	No abnormalities detected.
			pm	No abnormalities detected.
		8	am	No abnormalities detected.
			pm	No abnormalities detected.
		9	am	No abnormalities detected.
			pm	No abnormalities detected.
		10	am	No abnormalities detected.
			pm	No abnormalities detected.
		11	am	No abnormalities detected.
			pm	No abnormalities detected.
		12	am	No abnormalities detected.
			pm	Recovering from sedation.
		13	am	No abnormalities detected.
			pm	No abnormalities detected.
		14	am	Quiet but alert.
			pm	Quiet but alert.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
II (cont)	W546f (cont)	15	am	No abnormalities detected.
			pm	No abnormalities detected.
		16	am	Quiet but alert.
			pm	No abnormalities detected.
		17	am	No abnormalities detected.
			pm	No abnormalities detected.
		18	am	No abnormalities detected.
			pm	No abnormalities detected.
		19	am	No abnormalities detected.
			pm	No abnormalities detected.
		20	am	No abnormalities detected.
			pm	No abnormalities detected.
		21	am	No abnormalities detected.
			pm	No abnormalities detected.
		22	am	Quiet.
			pm	No abnormalities detected.
		23	am	No abnormalities detected.
			pm	No abnormalities detected.
		24	am	Quiet.
			pm	Quiet.
		25	am	No abnormalities detected.
			pm	Quiet.
		26	am	No abnormalities detected.
			pm	No abnormalities detected.
		27	am	No abnormalities detected.
			pm	No abnormalities detected.
		28	am	No abnormalities detected.
			pm	Sacrificed.
III	W542f	1	am	Quiet but alert.
			pm	No abnormalities detected.
		2	am	Alert and active.
			pm	Alert and active.
		3	am	Quiet, loose faeces, diet vomit in cage.
			pm	Quiet but alert.
		4	am	Quiet, loose faeces.
			pm	Quiet, loose faeces.
		5	am	Alert and active.
			pm	Quiet but alert. Loose faeces.
		6	am	Alert and active.
			pm	Quiet, huddled.
		7	am	Quiet.
			pm	Quiet.
		8	am	Quiet but alert.
			pm	No abnormalities detected.
		9	am	No abnormalities detected.
			pm	No abnormalities detected.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
III (cont)	W542f (cont)	10	am	No abnormalities detected.
			pm	No abnormalities detected.
		11	am	No abnormalities detected.
			pm	No abnormalities detected.
		12	am	No abnormalities detected.
			pm	No abnormalities detected.
		13	am	No abnormalities detected.
			pm	No abnormalities detected.
		14	am	Loose faeces.
			pm	No abnormalities detected.
		15	am	No abnormalities detected.
			pm	Alert and active.
		16	am	Alert and active.
			pm	No abnormalities detected.
		17	am	No abnormalities detected.
			pm	No abnormalities detected.
		18	am	No abnormalities detected.
			pm	No abnormalities detected.
		19	am	No abnormalities detected.
			pm	No abnormalities detected.
		20	am	No abnormalities detected.
			pm	No abnormalities detected.
		21	am	No abnormalities detected.
			pm	No abnormalities detected.
		22	am	No abnormalities detected.
			pm	No abnormalities detected.
		23	am	No abnormalities detected.
			pm	Quiet, huddled.
		24	am	No abnormalities detected.
			pm	No abnormalities detected.
		25	am	No abnormalities detected.
			pm	No abnormalities detected.
		26	am	No abnormalities detected.
			pm	No abnormalities detected.
		27	am	No abnormalities detected.
			pm	No abnormalities detected.
		28	am	Quiet.
			pm	Quiet but alert.
		29	am	Quiet but alert.
			pm	Quiet and huddled.
		30	am	Quiet and huddled.
			pm	Quiet but alert.
		31	am	Quiet and huddled but alert.
			pm	Quiet but alert.
		32	am	Quiet and huddled. Liquid faeces.
			pm	Quiet and huddled. Liquid faeces.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
III (cont)	W542f (cont)	33	am	Quiet but alert.
			pm	Quiet but alert.
		34	am	Quiet but alert.
			pm	Quiet but alert.
		35	am	No abnormalities detected.
			pm	No abnormalities detected.
		36	am	Quiet but alert.
			pm	Quiet but alert.
		37	am	Loose faeces.
			pm	Alert. No loose faeces seen.
		38	am	Quiet, loose faeces.
			pm	Quiet, loose faeces.
		39	am	Quiet, loose faeces.
			pm	Quiet, loose faeces.
		40	am	Quiet but alert.
			pm	Quiet but alert.
		41	am	Quiet but alert.
			pm	Sacrificed.
	W421m	1	am	Quiet but alert.
			pm	Quiet but alert, hunched posture, reluctant to move. Blood seeping from wound.
		2	am	Alert and active. Improved movement.
			pm	Quiet but alert.
		3	am	Quiet, loose faeces, diet vomit in cage.
			pm	Quiet but alert.
		4	am	No abnormalities detected.
			pm	No abnormalities detected.
		5	am	Comment not recorded.
			pm	Quiet but alert, loose faeces.
		6	am	Alert and active.
			pm	Quiet, huddled.
		7	am	No abnormalities detected.
			pm	No abnormalities detected.
		8	am	Quiet but alert, loose faeces.
			pm	No abnormalities detected.
		9	am	No abnormalities detected.
			pm	No abnormalities detected.
		10	am	No abnormalities detected.
			pm	No abnormalities detected.
		11	am	No abnormalities detected.
			pm	No abnormalities detected.
		12	am	No abnormalities detected.
			pm	No abnormalities detected.
		13	am	No abnormalities detected.
			pm	No abnormalities detected.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
III (cont)	W421m (cont)	14	am	No abnormalities detected.
			pm	No abnormalities detected.
		15	am	No abnormalities detected.
			pm	Alert and active.
		16	am	No abnormalities detected.
			pm	No abnormalities detected.
		17	am	Quiet but alert.
			pm	Quiet but alert.
		18	am	No abnormalities detected.
			pm	No abnormalities detected.
		19	am	No abnormalities detected.
			pm	No abnormalities detected.
		20	am	Loose faeces.
			pm	No abnormalities detected.
		21	am	No abnormalities detected.
			pm	No abnormalities detected.
		22	am	No abnormalities detected.
			pm	No abnormalities detected.
		23	am	No abnormalities detected.
			pm	Quiet, huddled.
		24	am	No abnormalities detected.
			pm	Quiet.
		25	am	No abnormalities detected.
			pm	No abnormalities detected.
		26	am	No abnormalities detected.
			pm	No abnormalities detected.
		27	am	No abnormalities detected.
			pm	No abnormalities detected.
		28	am	Quiet.
			pm	Quiet but alert.
		29	am	Quiet but alert.
			pm	Quiet and huddled.
		30	am	Quiet and huddled.
			pm	Quiet but alert.
		31	am	Quiet but alert.
			pm	Quiet but alert.
		32	am	Quiet and huddled.
			pm	Quiet and huddled.
		33	am	Quiet but alert.
			pm	Quiet but alert.
		34	am	No abnormalities detected.
			pm	No abnormalities detected.
		35	am	No abnormalities detected.
			pm	No abnormalities detected.
		36	am	No abnormalities detected.
			pm	No abnormalities detected.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
III (cont)	W421m (cont)	37	am	Loose faeces.
			pm	No loose faeces seen.
		38	am	Quiet but alert
			pm	Quiet but alert
		39	am	Alert and active, loose faeces.
			pm	Quiet, loose faeces.
		40	am	Quiet but alert.
			pm	Quiet but alert.
		41	am	No abnormalities detected.
			pm	Sacrificed.
	W289m	1	am	Quiet but alert.
			pm	Quiet but alert.
		2	am	Alert and active.
			pm	Alert and active.
		3	am	Quiet, loose faeces, diet vomit in cage.
			pm	Quiet but alert.
		4	am	Alert and active.
			pm	Alert and active.
		5	am	Alert and active.
			pm	Quiet but alert, loose faeces.
		6	am	Alert and active. Pale loose faeces.
			pm	Quiet, huddled.
		7	am	Quiet, loose faeces,
			pm	Quiet, loose faeces,
		8	am	Quiet but alert, loose faeces.
			pm	No abnormalities detected.
		9	am	No abnormalities detected.
			pm	No abnormalities detected.
		10	am	No abnormalities detected.
			pm	No abnormalities detected.
		11	am	No abnormalities detected.
			pm	No abnormalities detected.
		12	am	No abnormalities detected.
			pm	No abnormalities detected.
		13	am	No abnormalities detected.
			pm	No abnormalities detected.
		14	am	No abnormalities detected.
			pm	No abnormalities detected.
		15	am	No abnormalities detected.
			pm	Alert and active.
		16	am	Quiet.
			pm	No abnormalities detected.
		17	am	No abnormalities detected.
			pm	Quiet and huddled.
		18	am	No abnormalities detected.
			pm	No abnormalities detected.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
III (cont)	W289m (cont)	19	am	No abnormalities detected.
			pm	No abnormalities detected.
		20	am	No abnormalities detected.
			pm	No abnormalities detected.
		21	am	No abnormalities detected.
			pm	No abnormalities detected.
		22	am	No abnormalities detected.
			pm	No abnormalities detected.
		23	am	No abnormalities detected.
			pm	Quiet, huddled.
		24	am	No abnormalities detected.
			pm	No abnormalities detected.
		25	am	No abnormalities detected.
			pm	No abnormalities detected.
		26	am	No abnormalities detected.
			pm	No abnormalities detected.
		27	am	No abnormalities detected.
			pm	No abnormalities detected.
		28	am	Quiet.
			pm	Quiet.
		29	am	Quiet but alert.
			pm	Quiet and huddled.
		30	am	Quiet and huddled.
			pm	Quiet but alert.
		31	am	Quiet but alert.
			pm	Quiet but alert.
		32	am	Quiet and huddled.
			pm	Quiet and huddled.
		33	am	Quiet but alert.
			pm	Quiet but alert.
		34	am	Quiet but alert.
			pm	Quiet and huddled.
		35	am	No abnormalities detected.
			pm	No abnormalities detected.
		36	am	No abnormalities detected.
			pm	No abnormalities detected.
		37	am	Loose faeces.
			pm	No loose faeces seen.
		38	am	Alert and active.
			pm	Alert and active.
		39	am	Quiet, loose faeces.
			pm	Quiet, loose faeces.
		40	am	Quiet but alert.
			pm	Quiet but alert.
		41	am	Quiet but alert.
			pm	Sacrificed.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
III (cont)	W397m	1	am	Quiet but alert.
			pm	Quiet but alert.
		2	am	Alert and active.
			pm	Alert and active.
		3	am	Quiet, loose faeces, diet vomit in cage.
			pm	Quiet. Loose faeces.
		4	am	Quiet. Loose faeces.
			pm	Quiet. Loose faeces.
		5	am	Alert and active.
			pm	Quiet but alert, loose faeces.
		6	am	Alert and active.
			pm	Quiet, huddled.
		7	am	Quiet.
			pm	Quiet.
		8	am	Quiet but alert, loose faeces.
			pm	No abnormalities detected.
		9	am	No abnormalities detected.
			pm	No abnormalities detected.
		10	am	No abnormalities detected.
			pm	No abnormalities detected.
		11	am	No abnormalities detected.
			pm	No abnormalities detected.
		12	am	No abnormalities detected.
			pm	No abnormalities detected.
		13	am	No abnormalities detected.
			pm	No abnormalities detected.
		14	am	No abnormalities detected.
			pm	No abnormalities detected.
		15	am	No abnormalities detected.
			pm	Alert and active.
		16	am	No abnormalities detected.
			pm	No abnormalities detected.
		17	am	No abnormalities detected.
			pm	Quiet and huddled.
		18	am	No abnormalities detected.
			pm	No abnormalities detected.
		19	am	No abnormalities detected.
			pm	No abnormalities detected.
		20	am	No abnormalities detected.
			pm	No abnormalities detected.
		21	am	No abnormalities detected.
			pm	No abnormalities detected.
		22	am	No abnormalities detected.
			pm	No abnormalities detected.
		23	am	No abnormalities detected.
			pm	Quiet, huddled.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
III (cont)	W397m (cont)	24	am	No abnormalities detected.
			pm	No abnormalities detected.
		25	am	Quiet. Appears weak and unsteady.
			pm	Quiet and huddled.
		26	am	No abnormalities detected.
			pm	No abnormalities detected.
		27	am	No abnormalities detected.
			pm	No abnormalities detected.
		28	am	Quiet.
			pm	Quiet and huddled..
		29	am	Quiet but alert.
			pm	Very quiet and huddled.
		30	am	Quiet and huddled. Very dark loose faeces.
			pm	Quiet and huddled. Very dark loose faeces.
		31	am	Quiet but alert.
			pm	Quiet but alert.
		32	am	Quiet and huddled.
			pm	Quiet and huddled.
		33	am	Quiet and huddled.
			pm	Quiet but alert.
		34	am	Quiet and huddled.
			pm	Quiet and huddled.
		35	am	Quiet and huddled.
			pm	Quiet and huddled.
		36	am	Quiet and huddled.
			pm	Quiet and huddled.
		37	am	Quiet and huddled. Loose faeces.
			pm	Quiet. No loose faeces seen.
		38	am	Quiet but alert.
			pm	Quiet but alert.
		39	am	Alert and active, loose faeces.
			pm	Quiet, loose faeces.
		40	am	Quiet but alert.
			pm	Quiet but alert.
		41	am	Quiet but alert.
			pm	Sacrificed.
	W433m	1	am	Quiet but alert.
			pm	Quiet but alert.
		2	am	Alert and active.
			pm	Alert and active.
		3	am	Quiet, loose faeces, diet vomit in cage.
			pm	Quiet but alert.
		4	am	Quiet. Loose faeces.
			pm	Quiet. Loose faeces.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
III (cont)	W433m (cont)	5	am	No abnormalities detected.
			pm	Quiet but alert, loose faeces.
		6	am	Alert and active.
			pm	Quiet, huddled.
		7	am	Quiet.
			pm	Quiet.
		8	am	Quiet but alert, loose faeces.
			pm	No abnormalities detected.
		9	am	No abnormalities detected.
			pm	No abnormalities detected.
		10	am	No abnormalities detected.
			pm	No abnormalities detected.
		11	am	No abnormalities detected.
			pm	No abnormalities detected.
		12	am	No abnormalities detected.
			pm	No abnormalities detected.
		13	am	No abnormalities detected.
			pm	Quiet.
		14	am	Loose faeces.
			pm	No abnormalities detected.
		15	am	No abnormalities detected.
			pm	Alert and active.
		16	am	No abnormalities detected.
			pm	No abnormalities detected.
		17	am	No abnormalities detected.
			pm	No abnormalities detected.
		18	am	No abnormalities detected.
			pm	No abnormalities detected.
		19	am	No abnormalities detected.
			pm	No abnormalities detected.
		20	am	No abnormalities detected.
			pm	No abnormalities detected.
		21	am	No abnormalities detected.
			pm	No abnormalities detected.
		22	am	No abnormalities detected.
			pm	No abnormalities detected.
		23	am	No abnormalities detected.
			pm	Quiet, huddled.
		24	am	No abnormalities detected.
			pm	No abnormalities detected.
		25	am	No abnormalities detected.
			pm	No abnormalities detected.
		26	am	No abnormalities detected.
			pm	No abnormalities detected.
		27	am	No abnormalities detected.
			pm	No abnormalities detected.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
III (cont)	W433m (cont)	28	am	Quiet.
			pm	Quiet but alert.
		29	am	Quiet but alert.
			pm	Quiet but alert. Congested breathing.
		30	am	Quiet and huddled. Congested breathing.
			pm	Quiet but alert. Congested breathing.
		31	am	Quiet and huddled but alert.
			pm	Quiet but alert.
		32	am	Quiet and huddled.
			pm	Quiet and huddled.
		33	am	Quiet but alert
			pm	Quiet but alert.
		34	am	Quiet but alert.
			pm	Quiet but alert.
		35	am	No abnormalities detected.
			pm	No abnormalities detected.
		36	am	No abnormalities detected.
			pm	No abnormalities detected.
		37	am	Loose faeces.
			pm	No loose faeces seen.
		38	am	Quiet. Loose faeces.
			pm	Quiet. Loose faeces.
		39	am	Quiet, loose faeces.
			pm	Quiet, loose faeces.
		40	am	Quiet but alert.
			pm	Quiet but alert.
		41	am	Quiet but alert.
			pm	Sacrificed.
	W417m	1	am	Quiet but alert.
			pm	Quiet but alert.
		2	am	Alert and active.
			pm	Alert and active.
		3	am	Quiet, loose faeces, diet vomit in cage.
			pm	Quiet and huddled.
		4	am	Quiet. Loose faeces.
			pm	Quiet. Loose faeces.
		5	am	Comment not recorded.
			pm	Quiet but alert, loose faeces.
		6	am	Alert and active.
			pm	Quiet, huddled.
		7	am	No abnormalities detected.
			pm	No abnormalities detected.
		8	am	Quiet but alert, loose faeces.
			pm	No abnormalities detected.
		9	am	No abnormalities detected.
			pm	No abnormalities detected.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
III (cont)	W417m (cont)	10	am	No abnormalities detected.
			pm	No abnormalities detected.
		11	am	No abnormalities detected.
			pm	No abnormalities detected.
		12	am	No abnormalities detected.
			pm	No abnormalities detected.
		13	am	No abnormalities detected.
			pm	No abnormalities detected.
		14	am	No abnormalities detected.
			pm	No abnormalities detected.
		15	am	No abnormalities detected.
			pm	Alert and active.
		16	am	No abnormalities detected.
			pm	No abnormalities detected.
		17	am	Quiet but alert.
			pm	Quiet but alert.
		18	am	No abnormalities detected.
			pm	Loose faeces
		19	am	No abnormalities detected.
			pm	Loose faeces.
		20	am	No abnormalities detected.
			pm	No abnormalities detected.
		21	am	No abnormalities detected.
			pm	No abnormalities detected.
		22	am	No abnormalities detected.
			pm	No abnormalities detected.
		23	am	No abnormalities detected.
			pm	Quiet, huddled.
		24	am	Liquid faeces.
			pm	Liquid faeces.
		25	am	Loose faeces.
			pm	Loose faeces.
		26	am	Loose faeces.
			pm	Loose faeces.
		27	am	Loose faeces.
			pm	Sedated for biopsy.
		28	am	Quiet.
			pm	Quiet but alert.
		29	am	Quiet but alert.
			pm	Quiet but alert.
		30	am	Quiet and huddled.
			pm	Quiet but alert.
		31	am	Quiet but alert.
			pm	Quiet but alert.
		32	am	Quiet and huddled.
			pm	Quiet and huddled.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
III (cont)	W417m (cont)	33	am	Quiet and huddled.
			pm	Quiet but alert.
		34	am	Quiet but alert.
			pm	Quiet and huddled.
		35	am	Quiet and huddled.
			pm	Quiet and huddled.
		36	am	No abnormalities detected.
			pm	No abnormalities detected.
		37	am	Loose faeces.
			pm	No loose faeces seen.
		38	am	Quiet and huddled.
			pm	Quiet and huddled.
		39	am	Quiet, loose faeces.
			pm	Quiet, loose faeces.
		40	am	Quiet but alert.
			pm	Quiet but alert.
		41	am	Quiet but alert.
			pm	Sacrificed.
IV	W419m	1	am	Alert and active.
			pm	Quiet and huddled.
		2	am	Quiet but alert.
			pm	Quiet but alert.
		3	am	Loose faeces.
			pm	Loose faeces.
		4	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		5	am	Quiet but alert.
			pm	Quiet.
		6	am	Quiet but alert.
			pm	Quiet but alert.
		7	am	No abnormalities detected.
			pm	No abnormalities detected.
		8	am	No abnormalities detected.
			pm	No abnormalities detected.
		9	am	Quiet but alert.
			pm	No abnormalities detected.
		10	am	No abnormalities detected.
			pm	No abnormalities detected.
		11	am	Quiet.
			pm	No abnormalities detected.
		12	am	Quiet.
			pm	No abnormalities detected.
		13	am	No abnormalities detected.
			pm	No abnormalities detected.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
IV	W419 m	14	am	No abnormalities detected.
(cont)	(cont)		pm	No abnormalities detected.
		15	am	No abnormalities detected.
			pm	No abnormalities detected.
		16	am	Quiet.
			pm	Quiet but alert.
		17	am	Quiet but alert.
			pm	No abnormalities detected.
		18	am	Quiet but alert.
			pm	Quiet but alert.
		19	am	Quiet but alert.
			pm	Quiet but alert.
		20	am	No abnormalities detected.
			pm	No abnormalities detected.
		21	am	Quiet.
			pm	Quiet but alert. Observed sneezing.
		22	am	Quiet but alert.
			pm	Quiet but alert.
		23	am	Quiet but alert.
			pm	Quiet but alert.
		24	am	Quiet but alert. Observed sneezing. Clear nasal discharge.
			pm	Quiet and huddled.
		25	am	Quiet but alert.
			pm	Quiet and huddled.
		26	am	Quiet but alert.
			pm	Quiet and huddled.
		27	am	No abnormalities detected.
			pm	No abnormalities detected.
		28	am	No abnormalities detected.
			pm	No abnormalities detected.
		29	am	Quiet but alert.
			pm	No abnormalities detected.
		30	am	Quiet but alert.
			pm	Quiet but alert.
		31	am	Quiet. Liquid faeces.
			pm	Quiet. Liquid faeces.
		32	am	Quiet but alert.
			pm	Quiet but alert.
		33	am	Quiet and huddled.
			pm	Quiet and huddled.
		34	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert.
		35	am	Quiet and huddled.
			pm	Sedated for biopsy.
		36	am	Quiet and huddled.
			pm	Quiet and huddled.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
IV (cont)	W419m (cont)	37	am	Quiet and huddled.
			pm	Quiet and huddled on perch.
		38	am	Quiet and huddled.
			pm	Quiet and huddled.
		39	am	Quiet and huddled.
			pm	Quiet and huddled.
		40	am	Quiet and huddled.
			pm	Quiet and huddled.
		41	am	Quiet and huddled.
			pm	Quiet and huddled.
		42	am	Quiet but alert.
			pm	Quiet but alert.
		43	am	Quiet but alert.
			pm	Quiet but alert.
		44	am	Quiet and huddled.
			pm	Quiet and huddled. Occasionally active.
		45	am	Quiet but alert.
			pm	Quiet but alert.
		46	am	Alert and active.
			pm	Alert and active. Loose faeces.
		47	am	Alert and active. Loose/liquid faeces.
			pm	Quiet and huddled but alert.
		48	am	Quiet and huddled.
			pm	Quiet but alert.
		49	am	Quiet but alert. Liquid faeces.
			pm	Quiet but alert.
		50	am	Alert and active.
			pm	Alert and active.
		51	am	Quiet.
			pm	Quiet.
		52	am	Quiet but alert.
			pm	Quiet but alert.
		53	am	No abnormalities detected.
			pm	No abnormalities detected.
		54	am	Quiet.
			pm	Quiet.
		55	am	Quiet but alert.
			pm	Quiet but alert.
		56	am	Quiet but alert.
			pm	Quiet but alert.
		57	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		58	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Normal faeces.
		59	am	Quiet but alert.
			pm	Quiet but alert.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
IV (cont)	W419m (cont)	60	am	Alert and active. Loose faeces.
			pm	Alert and active. Loose faeces.
		61	am	Quiet but alert.
			pm	Quiet but alert.
		62	am	Quiet but alert.
			pm	Alert and active.
		63	am	Alert and active.
			pm	Alert and active.
		64	am	Alert and active. Liquid faeces.
			pm	Alert and active. Liquid faeces.
		65	am	Quiet but alert. Loose faeces.
			pm	Sacrificed.
	W615m	1	am	Quiet but alert.
			pm	Quiet and huddled.
		2	am	Quiet.
			pm	Quiet but alert.
		3	am	Loose faeces.
			pm	Loose faeces.
		4	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		5	am	Quiet but alert. Loose faeces.
			pm	Quiet.
		6	am	Quiet.
			pm	Quiet but alert.
		7	am	Quiet.
			pm	No abnormalities detected.
		8	am	Quiet.
			pm	No abnormalities detected.
		9	am	Quiet and huddled.
			pm	Quiet but alert.
		10	am	No abnormalities detected.
			pm	Loose faeces.
		11	am	Quiet.
			pm	Loose faeces.
		12	am	Quiet.
			pm	Quiet but alert.
		13	am	No abnormalities detected.
			pm	No abnormalities detected.
		14	am	Observed sneezing.
			pm	No abnormalities detected.
		15	am	No abnormalities detected.
			pm	No abnormalities detected.
		16	am	Quiet. Liquid faeces.
			pm	Quiet.
		17	am	Quiet but alert.
			pm	No abnormalities detected.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
IV (cont)	W615m (cont)	18	am	Quiet but alert.
			pm	Quiet but alert.
		19	am	Quiet.
			pm	Quiet but alert.
		20	am	No abnormalities detected.
			pm	No abnormalities detected.
		21	am	Quiet.
			pm	Quiet and huddled.
		22	am	Quiet and huddled. Loose faeces.
			pm	Quiet but alert.
		23	am	Quiet but alert.
			pm	Quiet but alert.
		24	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled.
		25	am	Quiet but alert.
			pm	Quiet and huddled.
		26	am	Quiet and huddled.
			pm	Quiet and huddled.
		27	am	No abnormalities detected.
			pm	No abnormalities detected.
		28	am	Quiet but alert.
			pm	Quiet but alert.
		29	am	Quiet and huddled.
			pm	Quiet and huddled.
		30	am	Quiet and huddled.
			pm	Quiet and huddled.
		31	am	Quiet. Loose faeces.
			pm	Quiet and huddled.
		32	am	Quiet but alert.
			pm	Quiet but alert.
		33	am	Quiet and huddled.
			pm	Quiet and huddled.
		34	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled.
		35	am	Quiet and huddled.
			pm	Quiet and huddled.
		36	am	Quiet and huddled but alert.
			pm	Quiet and huddled.
		37	am	Quiet and huddled.
			pm	Quiet and huddled on perch.
		38	am	Quiet and huddled.
			pm	Quiet and huddled.
		39	am	Quiet and huddled.
			pm	Quiet and huddled.
		40	am	Quiet and huddled.
			pm	Quiet and huddled.
		41	am	Quiet and huddled.
			pm	Quiet and huddled.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
IV (cont)	W615m (cont)	42	am	Quiet but alert.
			pm	No abnormalities detected.
		43	am	Quiet but alert.
			pm	Quiet but alert.
		44	am	Quiet and huddled.
			pm	Quiet and huddled. Occasionally active.
		45	am	Quiet but alert.
			pm	Quiet but alert.
		46	am	Quiet but alert.
			pm	Quiet but alert.
		47	am	Quiet but alert.
			pm	Quiet and huddled but alert.
		48	am	Quiet but alert.
			pm	Quiet but alert.
		49	am	Quiet but alert. Liquid faeces.
			pm	Quiet but alert.
		50	am	Alert and active.
			pm	Alert and active.
		51	am	Quiet.
			pm	Quiet.
		52	am	Quiet but alert.
			pm	Quiet but alert.
		53	am	Quiet.
			pm	Quiet but alert.
		54	am	Quiet.
			pm	Quiet.
		55	am	Quiet but alert.
			pm	Quiet but alert.
		56	am	Quiet but alert.
			pm	Quiet but alert.
		57	am	Quiet but alert.
			pm	Alert and active.
		58	am	Quiet but alert.
			pm	Quiet but alert.
		59	am	Quiet but alert.
			pm	Quiet but alert.
		60	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		61	am	Quiet but alert.
			pm	Quiet but alert.
		62	am	Quiet but alert.
			pm	Alert and active.
		63	am	Alert and active. Loose faeces.
			pm	Alert and active. Loose faeces.
		64	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert.
		65	am	Quiet but alert.
			pm	Sacrificed.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
IV (cont)	W612f	1	am	Quiet but alert.
			pm	Quiet and huddled.
		2	am	Quiet but alert.
			pm	Quiet but alert.
		3	am	No abnormalities detected.
			pm	No abnormalities detected.
		4	am	Quiet but alert.
			pm	Quiet but alert.
		5	am	Quiet but alert.
			pm	Quiet.
		6	am	Quiet but alert.
			pm	Quiet but alert.
		7	am	Quiet.
			pm	No abnormalities detected.
		8	am	Quiet.
			pm	No abnormalities detected.
		9	am	No abnormalities detected.
			pm	Quiet but alert.
		1	am	No abnormalities detected.
		0	pm	Loose faeces.
		1	am	Quiet.
		1	pm	Loose faeces.
		1	am	Quiet. Loose faeces.
		2	pm	Quiet but alert.
		1	am	No abnormalities detected.
		3	pm	No abnormalities detected.
		1	am	No abnormalities detected.
		4	pm	No abnormalities detected.
		1	am	No abnormalities detected.
		5	pm	No abnormalities detected.
		1	am	Quiet.
		6	pm	Quiet but alert.
		1	am	Quiet but alert.
		7	pm	No abnormalities detected.
		1	am	Quiet but alert.
		8	pm	Quiet but alert.
		1	am	Quiet.
		9	pm	Quiet but alert.
		2	am	No abnormalities detected.
		0	pm	No abnormalities detected.
		2	am	Quiet and huddled.
		1	pm	Quiet but alert.
			pm	Quiet but alert.
		2	am	Quiet and huddled.
		2	pm	Quiet but alert.
		2	am	Alert and active.
		3	pm	Quiet but alert.
		2	am	Quiet but alert. Loose faeces.
		4	pm	Quiet but alert.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
IV (cont)	W612f (cont)	25	am	Alert and active.
			pm	Quiet and huddled.
		26	am	Quiet but alert.
			pm	Quiet. Thin and dehydrated.
		27	am	Quiet and huddled.
			pm	Quiet and huddled.
		28	am	Quiet but alert.
			pm	Quiet but alert.
		29	am	Quiet and huddled. Loose faeces.
			pm	Quiet. Liquid faeces.
		30	am	Quiet. Liquid faeces.
			pm	Quiet. Liquid faeces.
		31	am	Quiet. Liquid faeces.
			pm	Quiet. Liquid faeces.
		32	am	Quiet. Liquid faeces.
			pm	Quiet. Liquid faeces.
		33	am	Quiet. Loose faeces.
			pm	Quiet and huddled.
		34	am	Quiet but alert.
			pm	Quiet but alert. Loose faeces.
		35	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled.
		36	am	Quiet and huddled.
			pm	Quiet and huddled.
		37	am	Quiet and huddled.
			pm	Quiet and huddled on perch.
		38	am	Quiet and huddled.
			pm	Quiet and huddled.
		39	am	Quiet and huddled.
			pm	Quiet and huddled.
		40	am	Quiet and huddled.
			pm	Quiet and huddled.
		41	am	Quiet and huddled.
			pm	Quiet and huddled.
		42	am	Quiet but alert.
			pm	Quiet but alert.
		43	am	Quiet but alert.
			pm	Quiet but alert.
		44	am	Quiet and huddled.
			pm	Quiet and huddled. Occasionally active.
		45	am	Quiet but alert.
			pm	Quiet but alert.
		46	am	Quiet but alert.
			pm	Quiet but alert.
		47	am	Quiet but alert.
			pm	Quiet and huddled but alert.
		48	am	Quiet but alert.
			pm	Quiet but alert.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
IV (cont)	W612f (cont)	49	am	Quiet but alert.
			pm	Quiet but alert.
		50	am	Alert and active.
			pm	Alert and active.
		51	am	Quiet.
			pm	Quiet.
		52	am	Quiet but alert.
			pm	Quiet but alert.
		53	am	Quiet.
			pm	Quiet.
		54	am	Quiet.
			pm	Quiet.
		55	am	Quiet but alert.
			pm	Quiet but alert.
		56	am	Quiet and huddled but alert.
			pm	Quiet but alert.
		57	am	Quiet but alert.
			pm	Quiet but alert.
		58	am	Quiet but alert.
			pm	Quiet but alert.
		59	am	Quiet but alert.
			pm	Quiet but alert.
		60	am	Quiet but alert.
			pm	Quiet but alert.
		61	am	Quiet but alert.
			pm	Quiet but alert.
		62	am	Quiet but alert.
			pm	Alert and active.
		63	am	Quiet but alert.
			pm	Quiet but alert.
		64	am	Quiet but alert.
			pm	Quiet but alert.
		65	am	Quiet but alert. Sacrificed
	W634f	1	am	Quiet but alert.
			pm	Quiet and huddled.
		2	am	Quiet but alert.
			pm	Quiet but alert.
		3	am	No abnormalities detected.
			pm	No abnormalities detected.
		4	am	Quiet but alert.
			pm	Quiet but alert.
		5	am	Quiet but alert.
			pm	Quiet.
		6	am	Quiet but alert.
			pm	Quiet but alert.
		7	am	Quiet.
			pm	No abnormalities detected.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
IV (cont)	W634f (cont)	8	am	Quiet.
			pm	No abnormalities detected.
		9	am	Quiet.
			pm	Quiet but alert.
		10	am	No abnormalities detected.
			pm	No abnormalities detected.
		11	am	Quiet.
			pm	No other abnormalities detected.
		12	am	No other abnormalities detected.
			pm	Quiet but alert.
		13	am	No abnormalities detected.
			pm	No abnormalities detected.
		14	am	No abnormalities detected.
			pm	No abnormalities detected.
		15	am	No abnormalities detected.
			pm	No abnormalities detected.
		16	am	No abnormalities detected.
			pm	Quiet but alert..
		17	am	Quiet but alert.
			pm	No abnormalities detected.
		18	am	Quiet but alert.
			pm	Quiet but alert.
		19	am	Quiet.
			pm	Quiet but alert.
		20	am	No abnormalities detected.
			pm	No abnormalities detected.
		21	am	Quiet and huddled.
			pm	Quiet but alert.
		22	am	Quiet and huddled.
			pm	Quiet but alert.
		23	am	No abnormalities detected.
			pm	Quiet but alert.
		24	am	Quiet and huddled. Slow laboured movement. Loose faeces.
			pm	Quiet and huddled.
		25	am	Alert and active.
			pm	Quiet and huddled.
		26	am	Quiet and huddled.
			pm	Quiet and huddled.
		27	am	Quiet and huddled.
			pm	Quiet and huddled.
		28	am	Quiet and huddled.
			pm	Quiet and huddled.
		29	am	Quiet and huddled.
			pm	Quiet but alert. Liquid faeces.
		30	am	Quiet. Liquid faeces.
			pm	Quiet. Liquid faeces.
		31	am	Quiet. Liquid faeces.
			pm	Quiet. Liquid faeces.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
IV (cont)	W634f (cont)	32	am	Quiet. Liquid faeces.
			pm	Quiet. Liquid faeces.
		33	am	Quiet. Loose faeces.
			pm	Quiet and huddled.
		34	am	Quiet but alert.
			pm	Quiet and huddled. Loose faeces.
		35	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled.
		36	am	Quiet and huddled.
			pm	Quiet and huddled.
		37	am	Quiet and huddled. Grating teeth. Loose faeces.
			pm	Quiet and huddled on perch.
		38	am	Quiet and huddled.
			pm	Quiet and huddled.
		39	am	Quiet and huddled.
			pm	Quiet and huddled.
		40	am	Quiet and huddled.
			pm	Quiet and huddled.
		41	am	Quiet and huddled.
			pm	Quiet and huddled.
		42	am	Quiet but alert.
			pm	Quiet but alert.
		43	am	Quiet but alert.
			pm	Quiet but alert.
		44	am	Quiet and huddled.
			pm	Quiet and huddled. Occasionally active.
		45	am	Quiet but alert.
			pm	Quiet but alert.
		46	am	Alert and active.
			pm	Quiet but alert.
		47	am	Quiet but alert.
			pm	Quiet and huddled but alert.
		48	am	Quiet but alert.
			pm	Quiet but alert.
		49	am	Quiet but alert.
			pm	Quiet but alert.
		50	am	Alert and active.
			pm	Alert and active.
		51	am	Quiet.
			pm	Quiet.
		52	am	Quiet but alert.
			pm	Quiet but alert.
		53	am	Quiet.
			pm	Quiet.
		54	am	Quiet.
			pm	Quiet.
		55	am	Quiet but alert.
			pm	Quiet but alert.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
IV (cont)	W634f (cont)	56	am	Quiet but alert.
			pm	Quiet but alert.
		57	am	Quiet but alert.
			pm	Quiet but alert.
		58	am	Quiet and huddled. Loose faeces..
			pm	Quiet but alert.
		59	am	Quiet but alert.
			pm	Quiet but alert.
		60	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		61	am	Quiet but alert.
			pm	Quiet but alert.
		62	am	Quiet but alert.
			pm	Alert and active.
		63	am	Alert and active.
			pm	Alert and active.
		64	am	Alert and active.
			pm	Alert and active.
		65	am	Quiet but alert. Sacrificed.
	W742m	1	am	Quiet but alert.
			pm	Quiet and huddled.
		2	am	Quiet.
			pm	Quiet but alert.
		3	am	No abnormalities detected.
			pm	No abnormalities detected.
		4	am	Quiet but alert.
			pm	Quiet but alert.
		5	am	Quiet but alert.
			pm	Quiet.
		6	am	Quiet.
			pm	Quiet but alert.
		7	am	Quiet.
			pm	No abnormalities detected.
		8	am	Quiet.
			pm	No abnormalities detected.
		9	am	Quiet. Loose faeces.
			pm	Quiet but alert.
		10	am	No abnormalities detected.
			pm	Liquid faeces.
		11	am	Quiet. Liquid faeces.
			pm	Quiet. Liquid faeces.
		12	am	Quiet. Liquid/loose faeces.
			pm	Quiet but alert.
		13	am	No abnormalities detected.
			pm	No abnormalities detected.
		14	am	No abnormalities detected.
			pm	No abnormalities detected.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
IV (cont)	W742m (cont)	15	am	No abnormalities detected.
			pm	No abnormalities detected.
		16	am	Quiet.
			pm	Quiet but alert.
		17	am	Quiet but alert.
			pm	No abnormalities detected.
		18	am	Quiet but alert.
			pm	Quiet but alert.
		19	am	Quiet.
			pm	Quiet but alert.
		20	am	No abnormalities detected.
			pm	No abnormalities detected.
		21	am	Quiet.
			pm	Quiet but alert.
		22	am	Quiet and huddled.
			pm	Quiet and huddled.
		23	am	Quiet but alert.
			pm	Quiet but alert.
		24	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled.
		25	am	Quiet but alert.
			pm	Quiet and huddled.
		26	am	Quiet but alert.
			pm	Quiet and huddled. Sneezing.
		27	am	No abnormalities detected.
			pm	No abnormalities detected.
		28	am	Quiet but alert. Liquid faeces.
			pm	Quiet but alert. Liquid faeces.
		29	am	Quiet and huddled.
			pm	Quiet and huddled.
		30	am	Quiet and huddled.
			pm	Quiet and huddled.
		31	am	Quiet. Liquid faeces.
			pm	Alert and active. Liquid faeces.
		32	am	Quiet. Liquid faeces.
			pm	Quiet. Liquid faeces.
		33	am	Quiet and huddled. Liquid faeces.
			pm	Quiet and huddled. Liquid faeces.
		34	am	Quiet and huddled.
			pm	Quiet and huddled.
		35	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled.
		36	am	Quiet and huddled but alert.
			pm	Quiet and huddled.
		37	am	Quiet and huddled.
			pm	Quiet and huddled.
		38	am	Quiet and huddled.
			pm	Quiet and huddled.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
IV (cont)	W742m (cont)	39	am	Quiet and huddled.
			pm	Quiet and huddled.
		40	am	Quiet and huddled.
			pm	Quiet and huddled.
		41	am	Quiet and huddled.
			pm	Quiet and huddled.
		42	am	Quiet but alert.
			pm	Quiet but alert.
		43	am	Quiet but alert.
			pm	Quiet but alert.
		44	am	Quiet and huddled.
			pm	Quiet and huddled. Occasionally active.
		45	am	Quiet but alert.
			pm	Quiet but alert.
		46	am	Quiet but alert.
			pm	Quiet but alert.
		47	am	Quiet but alert.
			pm	Quiet and huddled but alert.
		48	am	Quiet but alert.
			pm	Quiet but alert.
		49	am	Quiet but alert. Liquid faeces.
			pm	Quiet but alert.
		50	am	Alert and active.
			pm	Alert and active.
		51	am	Quiet.
			pm	Quiet.
		52	am	Quiet but alert.
			pm	Quiet but alert.
		53	am	Quiet but alert.
			pm	Quiet but alert.
		54	am	Quiet.
			pm	Quiet.
		55	am	Quiet but alert.
			pm	Quiet but alert.
		56	am	Quiet but alert.
			pm	Quiet but alert.
		57	am	Quiet and huddled.
			pm	Quiet and huddled.
		58	am	Quiet and huddled.
			pm	Quiet and huddled.
		59	am	Quiet and huddled. Lower lip bruised and swollen.
			pm	Quiet and huddled. Lower lip bruised and swollen.
		60	am	Quiet and huddled.
			pm	Quiet and huddled.
		61	am	Quiet but alert.
			pm	Quiet but alert.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
IV (cont)	W742f (cont)	62	am	Quiet but alert.
			pm	Alert and active.
		63	am	Quiet but alert.
			pm	Quiet but alert.
		64	am	Quiet but alert.
			pm	Alert and active.
		65	am	Quiet but alert. Sacrificed.
	W607m	1	am	Quiet and huddled.
			pm	Quiet and huddled.
		2	am	Quiet but alert.
			pm	Quiet but alert.
		3	am	Quiet but alert.
			pm	Quiet but alert.
		4	am	Quiet but alert.
			pm	Quiet.
		5	am	No abnormalities detected.
			pm	No abnormalities detected.
		6	am	Quiet.
			pm	No abnormalities detected.
		7	am	Quiet.
			pm	No abnormalities detected.
		8	am	No abnormalities detected.
			pm	Quiet but alert.
		9	am	No abnormalities detected.
			pm	No abnormalities detected.
		10	am	Quiet.
			pm	Quiet.
		11	am	Quiet.
			pm	Quiet.
		12	am	No abnormalities detected.
			pm	No abnormalities detected.
		13	am	No abnormalities detected.
			pm	No abnormalities detected.
		14	am	No abnormalities detected.
			pm	No abnormalities detected.
		15	am	Quiet.
			pm	Quiet but alert.
		16	am	Quiet but alert.
			pm	No abnormalities detected.
		17	am	Quiet but alert.
			pm	Alert.
		18	am	Quiet.
			pm	Quiet but alert.
		19	am	No abnormalities detected.
			pm	No abnormalities detected.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
IV (cont)	W607m (cont)	20	am	Quiet.
			pm	Quiet and huddled.
		21	am	Quiet and huddled.
			pm	Quiet but alert.
		22	am	Quiet but alert.
			pm	Quiet but alert.
		23	am	Quiet but alert.
			pm	Quiet and huddled.
		24	am	Alert and active.
			pm	Quiet and huddled.
		25	am	Quiet but alert.
			pm	Quiet and huddled.
		26	am	No abnormalities detected.
			pm	No abnormalities detected.
		27	am	No abnormalities detected.
			pm	No abnormalities detected.
		28	am	Quiet and huddled.
			pm	No abnormalities detected.
		29	am	Quiet but alert.
			pm	Quiet but alert.
		30	am	Quiet. Liquid faeces.
			pm	Quiet. Liquid faeces.
		31	am	Quiet but alert.
			pm	Quiet but alert.
		32	am	Quiet. Loose faeces.
			pm	Alert and active. Normal faeces.
		33	am	Quiet and huddled. Loose faeces. Sneezing.
			pm	Quiet and huddled.
		34	am	Quiet and huddled. Loose faeces.
			pm	Sedated for biopsy.
		35	am	Quiet and huddled.
			pm	Quiet and huddled.
		36	am	Quiet and huddled.
			pm	Quiet and huddled on perch.
		37	am	Quiet and huddled.
			pm	Quiet and huddled .
		38	am	Quiet and huddled.
			pm	Quiet and huddled.
		39	am	Quiet and huddled.
			pm	Quiet and huddled.
		40	am	Quiet and huddled.
			pm	Quiet and huddled.
		41	am	Quiet but alert.
			pm	Quiet but alert.
		42	am	Quiet but alert.
			pm	Quiet but alert.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
IV (cont)	W607m (cont)	43	am	Quiet and huddled.
			pm	Quiet and huddled. Occasionally active.
		44	am	Quiet but alert.
			pm	Quiet but alert.
		45	am	Alert and active.
			pm	Alert and active.
		46	am	Quiet but alert.
			pm	Quiet and huddled but alert.
		47	am	Quiet but alert.
			pm	Quiet but alert.
		48	am	Quiet but alert.
			pm	Quiet but alert.
		49	am	Alert and active.
			pm	Alert and active.
		50	am	Quiet.
			pm	Quiet.
		51	am	Quiet but alert.
			pm	Quiet but alert.
		52	am	No abnormalities detected.
			pm	No abnormalities detected.
		53	am	Quiet.
			pm	Quiet.
		54	am	Quiet but alert.
			pm	Quiet but alert.
		55	am	Quiet but alert.
			pm	Quiet but alert.
		56	am	Alert and active.
			pm	Alert and active.
		57	am	Alert and active.
			pm	Alert and active.
		58	am	Alert and active.
			pm	Alert and active.
		59	am	Alert and active.
			pm	Alert and active.
		60	am	Quiet but alert.
			pm	Quiet but alert.
		61	am	Quiet but alert.
			pm	Alert and active.
		62	am	Alert and active.
			pm	Alert and active.
		63	am	Alert and active.
			pm	Alert and active.
		64	am	Quiet but alert.
			pm	Sacrificed

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
V	W773m	1	am	Quiet but alert.
			pm	Quiet.
		2	am	Quiet.
			pm	Quiet, piloerection.
		3	am	Quiet.
			pm	Quiet.
		4	am	Quiet but alert.
			pm	Quiet but alert.
		5	am	Quiet but alert.
			pm	Quiet but alert.
		6	am	Quiet but alert.
			pm	Quiet.
		7	am	Quiet.
			pm	Quiet.
		8	am	Quiet.
			pm	Quiet but alert.
		9	am	Quiet but alert.
			pm	Quiet but alert.
		10	am	Alert and active.
			pm	Alert and active.
		11	am	Loose faeces.
			pm	Alert and active.
		12	am	Alert and active.
			pm	Alert and active.
		13	am	Alert and active.
			pm	Alert and active.
		14	am	No abnormalities detected.
			pm	No abnormalities detected.
		15	am	No abnormalities detected.
			pm	No abnormalities detected.
		16	am	No abnormalities detected.
			pm	No abnormalities detected.
		17	am	Quiet and huddled. Dark faeces.
			pm	Quiet and huddled. Dark faeces.
		18	am	No abnormalities detected.
			pm	Alert and active.
		19	am	Alert and active.
			pm	Alert and active.
		20	am	Alert and active.
			pm	Alert and active.
		21	am	No abnormalities detected.
			pm	No abnormalities detected.
		22	am	No abnormalities detected.
			pm	No abnormalities detected.
		23	am	No abnormalities detected.
			pm	Quiet and huddled but alert.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
V (cont)	W773m (cont)	24	am	No abnormalities detected.
			pm	No abnormalities detected.
		25	am	Alert and active.
			pm	Alert and active.
		26	am	No abnormalities detected.
			pm	Quiet but alert.
		27	am	No abnormalities detected.
			pm	Alert and active.
		28	am	Alert and active.
			pm	Alert and active.
		29	am	Alert and active.
			pm	No abnormalities detected.
		30	am	No abnormalities detected.
			pm	No abnormalities detected.
		31	am	No abnormalities detected.
			pm	No abnormalities detected.
		32	am	No abnormalities detected.
			pm	No abnormalities detected.
		33	am	No abnormalities detected.
			pm	No abnormalities detected.
		34	am	No abnormalities detected.
			pm	Quiet but alert.
		35	am	Quiet but alert.
			pm	Quiet but alert.
		36	am	Quiet but alert.
			pm	Quiet but alert.
		37	am	No abnormalities detected.
			pm	Recovering from sedation.
		38	am	Quiet but alert.
			pm	Quiet but alert.
		39	am	Quiet and huddled but alert.
			pm	Quiet and huddled but alert.
		40	am	Quiet but alert.
			pm	Quiet but alert.
		41	am	Quiet but alert.
			pm	Quiet but alert.
		42	am	Quiet but alert.
			pm	Quiet but alert.
		43	am	Quiet but alert.
			pm	Alert and active.
		44	am	Quiet but alert.
			pm	Alert and active.
		45	am	Alert and active.
			pm	Alert and active.
		46	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex		Day	Clinical signs
V (cont)	W773m (cont)	47	am	Quiet but alert. Loose faeces.
			pm	Alert and active.
		48	am	Quiet but alert.
			pm	Quiet but alert.
		49	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert.
		50	am	Quiet but alert.
			pm	Quiet but alert.
		51	am	Quiet but alert.
			pm	Quiet but alert.
		52	am	Quiet and huddled.
			pm	Quiet and huddled.
		53	am	Quiet but alert.
			pm	Quiet and huddled.
		54	am	Quiet but alert.
			pm	Quiet but alert.
		55	am	Quiet but alert. Loose faeces.
			pm	Alert and active. Normal faeces.
		56	am	Quiet but alert.
			pm	Alert and active.
		57	am	Alert and active.
			pm	Alert and active.
		58	am	Alert and active.
			pm	Alert and active.
		59	am	Alert and active.
			pm	Alert and active.
		60	am	Alert and active.
			pm	Alert and active.
		61	am	Comment not recorded.
			pm	No abnormalities detected.
		62	am	No abnormalities detected.
			pm	Quiet but alert.
		63	am	Alert and active.
			pm	Alert and active.
		64	am	Quiet but alert.
			pm	Quiet but alert.
		65	am	Quiet but alert.
			pm	Quiet but alert.
		66	am	Quiet but alert.
			pm	Quiet but alert.
		67	am	Loose faeces.
			pm	Quiet.
		68	am	Loose faeces.
			pm	Quiet.
		69	am	Quiet. Loose faeces.
			pm	Quiet.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
V (cont)	W733m (cont)	70	am	Quiet but alert.
			pm	Quiet. Loose faeces.
		71	am	Quiet but alert. Normal faeces.
			pm	Quiet but alert.
		72	am	Quiet but alert.
			pm	Quiet but alert.
		73	am	Quiet but alert.
			pm	Quiet and huddled.
		74	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		75	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		76	am	Quiet but alert. Liquid faeces.
			pm	Quiet but alert. Liquid faeces.
		77	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		78	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		79	am	Quiet and huddled. Loose faeces.
			pm	No abnormalities detected.
		80	am	Comment not recorded.
			pm	Quiet.
		81	am	Quiet. Loose faeces.
			pm	Quiet. Loose faeces.
		82	am	Quiet. Loose faeces. Vomit in cage.
			pm	Quiet. Loose faeces. Vomit in cage.
		83	am	Quiet but alert. Loose faeces.
			pm	Alert and active. Loose faeces.
		84	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		85	am	Quiet but alert. Loose faeces.
			pm	Quiet. Liquid faeces.
		86	am	Quiet. Liquid faeces.
			pm	Quiet. Liquid faeces.
		87	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert.
		88	am	Quiet but alert. Normal faeces.
			pm	Quiet but alert.
		89	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		90	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		91	am	Quiet but alert.
			pm	Quiet but alert.
		92	am	Quiet. Normal faeces.
			pm	Alert and active.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
V (cont)	W773m (cont)	93	am	Quiet but alert.
			pm	Alert and active.
		94	am	Alert and active.
			pm	Quiet but alert.
		95	am	Quiet but alert.
			pm	Quiet but alert.
		96	am	Quiet but alert.
			pm	Quiet but alert.
		97	am	Alert and active.
			pm	Alert and active.
		98	am	No abnormalities detected.
			pm	Sacrificed.
	W746f	1	am	Quiet but alert.
			pm	Quiet but alert.
		2	am	Quiet but alert.
			pm	Quiet but alert.
		3	am	Alert and active.
			pm	Alert and active.
		4	am	Alert and active..
			pm	Alert and active.
		5	am	Alert and active.
			pm	Alert and active.
		6	am	Alert and active.
			pm	Alert and active.
		7	am	No abnormalities detected.
			pm	No abnormalities detected.
		8	am	No abnormalities detected.
			pm	No abnormalities detected.
		9	am	No abnormalities detected.
			pm	No abnormalities detected.
		10	am	Quiet and huddled. Dark faeces.
			pm	Quiet and huddled. Dark faeces.
		11	am	No abnormalities detected.
			pm	Alert and active.
		12	am	Alert and active.
			pm	Alert and active.
		13	am	Alert and active.
			pm	Alert and active.
		14	am	No abnormalities detected.
			pm	No abnormalities detected.
		15	am	No abnormalities detected.
			pm	No abnormalities detected.
		16	am	No abnormalities detected.
			pm	Quiet and huddled but alert.
		17	am	No abnormalities detected.
			pm	No abnormalities detected.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
V (cont)	W746f (cont)	18	am	Alert and active.
			pm	Alert and active.
		19	am	No abnormalities detected.
			pm	No abnormalities detected.
		20	am	Alert and active.
			pm	No abnormalities detected.
		21	am	Alert and active.
			pm	Quiet but alert.
		22	am	Alert and active.
			pm	Alert and active.
		23	am	No abnormalities detected.
			pm	No abnormalities detected.
		24	am	No abnormalities detected.
			pm	No abnormalities detected.
		25	am	No abnormalities detected.
			pm	No abnormalities detected.
		26	am	No abnormalities detected.
			pm	No abnormalities detected.
		27	am	No abnormalities detected.
			pm	Quiet but alert.
		28	am	Quiet but alert.
			pm	Quiet but alert.
		29	am	Quiet but alert.
			pm	Quiet but alert.
		30	am	No abnormalities detected.
			pm	Recovering from sedation.
		31	am	Quiet but alert.
			pm	Quiet but alert.
		32	am	Quiet but alert.
			pm	Quiet but alert.
		33	am	Quiet. Slow movement around cage.
			pm	Quiet. Slow movement around cage.
		34	am	Quiet but alert.
			pm	Quiet but alert.
		35	am	Quiet and huddled.
			pm	Quiet and huddled.
		36	am	Quiet but alert.
			pm	Alert and active. Loose faeces.
		37	am	Quiet and huddled. Liquid faeces.
			pm	Quiet and huddled. Liquid faeces.
		38	am	Quiet and huddled. Unsteady. Loose faeces.
			pm	Quiet and huddled. Unsteady. Loose faeces.
		39	am	Quiet and huddled. Unsteady. Loose faeces.
			pm	Quiet and huddled. Unsteady. Loose faeces.
		40	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
V (cont)	W746f (cont)	41	am	Quiet but alert.
			pm	Quiet but alert.
		42	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert.
		43	am	Quiet but alert.
			pm	Quiet and huddled.
		44	am	Quiet but alert.
			pm	Quiet but alert.
		45	am	Quiet but alert.
			pm	Quiet but alert.
		46	am	Quiet but alert.
			pm	Quiet and huddled.
		47	am	Quiet but alert.
			pm	Quiet but alert.
		48	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		49	am	Quiet but alert. Liquid faeces.
			pm	Alert and active.
		50	am	Quiet but alert. Liquid faeces.
			pm	Alert and active. Liquid faeces.
		51	am	Quiet but alert. Liquid faeces.
			pm	Quiet but alert. Liquid faeces.
		52	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		53	am	Quiet but alert. Occasionally huddled. Normal faeces.
			pm	Quiet but alert. Occasionally huddled.
		54	am	Comment not recorded.
			pm	No abnormalities detected.
		55	am	Quiet.
			pm	Quiet but alert.
		56	am	Quiet but alert. .
			pm	Quiet but alert.
		57	am	Quiet but alert.
			pm	Quiet but alert. .
		58	am	Quiet but alert.
			pm	Quiet but alert.
		59	am	Quiet but alert. .
			pm	Quiet but alert.
		60	am	Loose faeces.
			pm	Quiet.
		61	am	Quiet but alert. Loose faeces.
			pm	Quiet.
		62	am	Quiet. Loose faeces.
			pm	Quiet. Normal faeces.
		63	am	Quiet and huddled. Loose faeces.
			pm	Quiet. Loose/liquid faeces.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
V (cont)	W746f (cont)	64	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		65	am	Quiet. Loose faeces. Swelling around eyes.
			pm	Quiet. Loose faeces. Swelling around eyes.
		66	am	Quiet. Loose faeces.
			pm	Quiet and huddled.
		67	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		68	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces. Swelling around both eyes.
		69	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		70	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		71	am	Quiet but alert. Loose faeces. Swelling around both eyes.
			pm	Quiet but alert. Loose faeces. Swelling around both eyes.
		72	am	Quiet but alert. Loose faeces. Swelling around both eyes.
			pm	Quiet but alert. Swelling around both eyes.
		73	am	Comment not recorded.
			pm	Quiet. Swelling around both eyes.
		74	am	Quiet. Loose faeces.
			pm	Quiet. Loose faeces.
		75	am	Quiet. Loose faeces. Vomit in tray.
			pm	Quiet. Loose faeces. Vomit in tray.
		76	am	Quiet but alert. Loose faeces. Swelling around both eyes.
			pm	Quiet and huddled. Loose faeces. Swelling around both eyes.
		77	am	Quiet but alert. Loose faeces. Swelling around both eyes.
			pm	Quiet but alert. Loose faeces. Swelling around both eyes.
		78	am	Quiet but alert. Loose faeces. Swelling around both eyes.
			pm	Quiet. Loose faeces.
		79	am	Quiet. Loose faeces.
			pm	Quiet. Loose faeces.
		80	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		81	am	Quiet but alert. Normal faeces.
			pm	Quiet but alert. Loose faeces.
		82	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Normal faeces.
		83	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		84	am	Quiet but alert. Normal faeces.
			pm	Quiet but alert.
		85	am	Quiet but alert.
			pm	Quiet but alert.
		86	am	Quiet but alert.
			pm	Alert and active.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
V (cont)	W746f (cont)	87	am	Quiet but alert.
			pm	Quiet and huddled.
		88	am	Quiet but alert.
			pm	Quiet but alert.
		89	am	Quiet but alert.
			pm	Quiet but alert.
		90	am	Alert and active.
			pm	Alert and active.
		91	am	No abnormalities detected.
			pm	Sacrificed.
	W766f	1	am	Quiet but alert.
			pm	Quiet and huddled but alert.
		2	am	No abnormalities detected.
			pm	No abnormalities detected.
		3	am	Alert and active.
			pm	Alert and active.
		4	am	No abnormalities detected.
			pm	No abnormalities detected.
		5	am	Alert and active.
			pm	No abnormalities detected.
		6	am	Alert and active.
			pm	Alert and active.
		7	am	Alert and active.
			pm	Alert and active.
		8	am	Alert and active.
			pm	Alert and active.
		9	am	Alert and active.
			pm	No abnormalities detected.
		10	am	Loose faeces.
			pm	No abnormalities detected. Normal faeces.
		11	am	Loose faeces.
			pm	Quiet but alert. Congested breathing.
		12	am	No abnormalities detected.
			pm	Quiet but alert.
		13	am	Quiet but alert.
			pm	Quiet but alert.
		14	am	Quiet but alert.
			pm	Quiet but alert.
		15	am	No abnormalities detected.
			pm	No abnormalities detected.
		16	am	No abnormalities detected.
			pm	No abnormalities detected.
		17	am	Quiet but alert.
			pm	Quiet but alert.
		18	am	No abnormalities detected.
			pm	No abnormalities detected.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
V (cont)	W766f (cont)	19	am	Quiet but alert.
			pm	Quiet but alert.
		20	am	No abnormalities detected.
			pm	No abnormalities detected.
		21	am	No abnormalities detected.
			pm	Alert and active.
		22	am	Quiet and huddled.
			pm	Quiet but alert.
		23	am	Quiet but alert.
			pm	Quiet but alert.
		24	am	Quiet but alert.
			pm	Quiet but alert.
		25	am	Alert and active.
			pm	Alert and active.
		26	am	Quiet but alert.
			pm	Quiet but alert.
		27	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert.
		28	am	Alert and active.
			pm	No abnormalities detected.
		29	am	Alert and active.
			pm	Alert and active.
		30	am	Quiet and huddled.
			pm	Quiet and huddled.
		31	am	Quiet but alert.
			pm	Quiet and huddled.
		32	am	Quiet but alert.
			pm	Quiet but alert.
		33	am	Quiet but alert. Loose faeces.
			pm	Animal in theatre.
		34	am	Quiet but alert.
			pm	Alert and active.
		35	am	Alert and active.
			pm	Alert and active.
		36	am	Alert and active.
			pm	Alert and active.
		37	am	Alert and active.
			pm	Alert and active.
		38	am	Alert and active.
			pm	Alert and active. Loose faeces.
		39	am	Comment not recorded.
			pm	No abnormalities detected.
		40	am	No abnormalities detected.
			pm	Loose faeces.
		41	am	Alert and active. Liquid faeces.
			pm	Quiet but alert.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
V (cont)	W766f (cont)	42	am	Quiet but alert.
			pm	Quiet but alert.
		43	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert.
		44	am	Quiet but alert.
			pm	Quiet but alert.
		45	am	Quiet but alert. Loose faeces.
			pm	Quiet.
		46	am	Quiet but alert. Loose faeces.
			pm	Quiet.
		47	am	Quiet.
			pm	Quiet.
		48	am	Quiet but alert. Loose faeces.
			pm	Quiet. Liquid faeces.
		49	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		50	am	Quiet. Loose faeces.
			pm	Quiet. Loose faeces.
		51	am	Quiet but alert. Loose faeces.
			pm	Quiet and huddled.
		52	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		53	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		54	am	Quiet but alert. Loose/liquid faeces.
			pm	Quiet but alert. Loose/liquid faeces.
		55	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		56	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		57	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. No loose faeces seen.
		58	am	Comment not recorded.
			pm	Quiet.
		59	am	Quiet. Loose faeces.
			pm	Quiet. Loose faeces.
		60	am	Quiet. Loose faeces. Vomit in cage.
			pm	Quiet. Loose faeces. Vomit in cage.
		61	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		62	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		63	am	Quiet but alert. Loose faeces.
			pm	Loose faeces.
		64	am	Quiet. Normal faeces.
			pm	Quiet.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
V (cont)	W766f (cont)	65	am	Quiet but alert.
			pm	Alert and active.
		66	am	Quiet but alert.
			pm	Quiet but alert. Loose faeces.
		67	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		68	am	Quiet but alert. Normal faeces.
			pm	Quiet but alert.
		69	am	Quiet but alert.
			pm	Quiet but alert.
		70	am	Quiet but alert.
			pm	Alert and active.
		71	am	Quiet but alert. Dark faeces.
			pm	Alert and active. Normal faeces.
		72	am	Quiet but alert.
			pm	Quiet but alert.
		73	am	Quiet.
			pm	Quiet.
		74	am	Quiet but alert. Dark faeces.
			pm	Quiet but alert. Dark faeces.
		75	am	Alert and active. Normal faeces.
			pm	Alert and active.
		76	am	No abnormalities detected.
			pm	Sacrificed.
VI	X34f	1	am	Quiet and huddled.
			pm	Quiet and huddled.
		2	am	Quiet and huddled.
			pm	Quiet and huddled.
		3	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		4	am	Quiet and huddled.
			pm	Quiet and huddled.
		5	am	Quiet but alert. Dark faeces.
			pm	Quiet but alert. Dark faeces.
		6	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		7	am	Quiet but alert. Loose faeces.
			pm	Quiet and huddled but alert. Loose faeces.
		8	am	Quiet and huddled. Loose/liquid faeces.
			pm	Quiet and huddled. Loose/liquid faeces.
		9	am	Quiet and huddled. Loose/liquid faeces.
			pm	Quiet and huddled. Loose/liquid faeces.
		10	am	Quiet and huddled. Loose/liquid faeces.
			pm	Quiet and huddled. Loose/liquid faeces.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
VI	X34f	11	am	Quiet and huddled. Loose/liquid faeces.
			pm	Quiet and huddled. Loose/liquid faeces.
		12	am	Quiet and huddled. Loose faeces. Vomit in cage.
			pm	Quiet and huddled. Loose faeces. Vomit in cage.
		13	am	Quiet but alert. Loose faeces.
			pm	Quiet and huddled.
		14	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		15	am	Quiet but alert. Loose faeces.
			pm	Quiet. Loose faeces.
		16	am	Quiet. Liquid faeces.
			pm	Quiet. Liquid faeces.
		17	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Normal faeces.
		18	am	Quiet but alert.
			pm	Quiet but alert.
		19	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		20	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		21	am	Quiet but alert. Normal faeces.
			pm	Quiet but alert.
		22	am	Quiet but alert.
			pm	Quiet but alert.
		23	am	Quiet but alert. Occasionally active.
			pm	Alert and active.
		24	am	Quiet but alert.
			pm	Quiet but alert.
		25	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		26	am	Quiet but alert. Normal faeces.
			pm	Quiet but alert.
		27	am	Alert and active.
			pm	Alert and active.
		28	am	Quiet but alert.
			pm	Quiet but alert.
		29	am	Quiet but alert. Occasionally active.
			pm	Quiet but alert.
		30	am	Quiet but alert. Occasionally active.
			pm	Quiet but alert.
		31	am	Quiet but alert.
			pm	Quiet but alert.
		32	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		33	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
IV (cont)	X34f (cont)	34	am	Quiet but alert.
			pm	Recovering from sedation.
		35	am	Quiet but alert and active.
			pm	Quiet but alert and active.
		36	am	Quiet but alert and active.
			pm	Quiet but alert and active.
		37	am	Quiet but alert.
			pm	Quiet but alert.
		38	am	Quiet but alert. Dark faeces.
			pm	Quiet but alert. Dark faeces.
		39	am	Quiet but alert. Dark faeces.
			pm	Quiet but alert. Dark faeces.
		40	am	Quiet but alert. Dark faeces.
			pm	Alert and active.
		41	am	Alert and active.
			pm	Alert and active.
		42	am	Alert and active.
			pm	Quiet and huddled.
		43	am	Quiet but alert.
			pm	Quiet but alert.
		44	am	Quiet but alert.
			pm	Quiet but alert.
		45	am	Quiet but alert and active.
			pm	Quiet but alert and active.
		46	am	Quiet but alert and active.
			pm	Swollen stomach wound seeping blood.
		47	am	Quiet.
			pm	Quiet but alert..
		48	am	Quiet but alert. Picking at wound.
			pm	Quiet but alert. Picking at wound.
		49	am	Quiet but alert. Picking at wound.
			pm	Quiet but alert. Picking at wound.
		50	am	Quiet but alert. Picking at wound.
			pm	Quiet but alert. Picking at wound.
		51	am	Picking at wound.
			pm	Picking at wound.
		52	am	Dark faeces.
			pm	Dark faeces.
		53	am	Dark faeces.
			pm	No abnormalities detected..
		54	am	Picking at wound.
			pm	Picking at wound.
		55	am	No abnormalities detected.
			pm	No abnormalities detected.
		56	am	No abnormalities detected.
			pm	No abnormalities detected.
		57	am	No abnormalities detected. Sacrificed.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
VI (cont)	X36f	1	am	Quiet and huddled.
			pm	Quiet and huddled.
		2	am	Quiet and huddled.
			pm	Quiet and huddled.
		3	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		4	am	Quiet and huddled.
			pm	Quiet and huddled.
		5	am	Quiet but alert. Dark faeces.
			pm	Quiet but alert. Dark faeces.
		6	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		7	am	Quiet but alert. Loose faeces.
			pm	Quiet and huddled but alert. Loose faeces.
		8	am	Quiet and huddled. Loose/liquid faeces.
			pm	Quiet and huddled. Loose/liquid faeces.
		9	am	Quiet and huddled. Loose/liquid faeces.
			pm	Quiet and huddled. Loose/liquid faeces.
		10	am	Quiet and huddled. Loose/liquid faeces.
			pm	Quiet and huddled. Loose/liquid faeces.
		11	am	Quiet and huddled. Loose/liquid faeces.
			pm	Quiet and huddled. Loose/liquid faeces.
		12	am	Quiet and huddled. Loose faeces. Vomit in cage.
			pm	Quiet and huddled. Loose faeces. Vomit in cage.
		13	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert.
		14	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		15	am	Quiet but alert. Loose faeces.
			pm	Quiet. Dark/loose faeces.
		16	am	Quiet. Dark faeces.
			pm	Quiet.
		17	am	Quiet but alert. Normal faeces.
			pm	Quiet but alert.
		18	am	Quiet but alert.
			pm	Quiet but alert.
		19	am	Quiet but alert.
			pm	Quiet but alert.
		20	am	Quiet but alert.
			pm	Quiet but alert.
		21	am	Quiet but alert.
			pm	Quiet but alert.
		22	am	Quiet but alert.
			pm	Quiet but alert.
		23	am	Quiet but alert. Occasionally active.
			pm	Alert and active.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
VI (cont)	X36f (cont)	24	am	Quiet but alert.
			pm	Quiet but alert.
		25	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		26	am	Quiet but alert. Normal faeces.
			pm	Quiet but alert. Normal faeces.
		27	am	Alert and active.
			pm	Alert and active.
		28	am	Quiet but alert.
			pm	Quiet but alert.
		29	am	Alert and active.
			pm	Alert and active.
		30	am	Alert and active.
			pm	Quiet but alert.
		31	am	Quiet but alert.
			pm	Quiet but alert.
		32	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Normal faeces.
		33	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		34	am	Quiet but alert.
			pm	Recovering from sedation.
		35	am	Quiet but alert and active.
			pm	Quiet but alert and active.
		36	am	Quiet but alert and active.
			pm	Quiet but alert and active.
		37	am	Quiet but alert.
			pm	Quiet but alert.
		38	am	Quiet but alert. Dark faeces.
			pm	Quiet but alert. Dark faeces.
		39	am	Quiet but alert. Dark faeces.
			pm	Quiet but alert. Dark faeces.
		40	am	Quiet but alert. Dark faeces.
			pm	Alert and active.
		41	am	Alert and active.
			pm	Alert and active.
		42	am	Alert and active.
			pm	Quiet but alert.
		43	am	Quiet but alert.
			pm	Quiet but alert.
		44	am	Quiet but alert.
			pm	Quiet but alert.
		45	am	Quiet but alert and active.
			pm	Quiet but alert and active.
		46	am	Quiet but alert and active.
			pm	Quiet but alert.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
VI (cont)	X36f (cont)	47	am	Quiet.
			pm	Quiet.
		48	am	Quiet.
			pm	Quiet.
		49	am	Alert and active.
			pm	No abnormalities detected.
		50	am	No abnormalities detected.
			pm	No abnormalities detected.
		51	am	No abnormalities detected.
			pm	No abnormalities detected.
		52	am	Dark faeces.
			pm	Dark faeces.
		53	am	Dark faeces.
			pm	No abnormalities detected.
		54	am	No abnormalities detected.
			pm	No abnormalities detected..
		55	am	No abnormalities detected.
			pm	No abnormalities detected.
		56	am	No abnormalities detected.
			pm	No abnormalities detected.
		57	am	No abnormalities detected. Sacrificed.
	X51m	1	am	Quiet and huddled.
			pm	Quiet and huddled.
		2	am	Quiet and huddled.
			pm	Quiet and huddled.
		3	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		4	am	Quiet and huddled.
			pm	Quiet and huddled.
		5	am	Quiet but alert. Dark faeces.
			pm	Quiet but alert. Dark faeces.
		6	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		7	am	Quiet but alert. Loose faeces.
			pm	Quiet and huddled but alert. Loose faeces.
		8	am	Quiet and huddled. Loose/liquid faeces.
			pm	Quiet and huddled. Loose/liquid faeces.
		9	am	Quiet and huddled. Loose/liquid faeces.
			pm	Quiet and huddled. Loose/liquid faeces.
		10	am	Quiet and huddled. Loose/liquid faeces.
			pm	Quiet and huddled. Loose/liquid faeces.
		11	am	Quiet and huddled. Loose/liquid faeces.
			pm	Quiet and huddled. Loose/liquid faeces.
		12	am	Quiet and huddled. Liquid faeces. Vomit in cage.
			pm	Quiet and huddled. Liquid faeces. Vomit in cage.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
VI (cont)	X51m (cont)	13	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert.
		14	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		15	am	Quiet but alert. Loose faeces.
			pm	Quiet. Normal faeces.
		16	am	Quiet. Dark/loose faeces.
			pm	Quiet. Loose faeces.
		17	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Normal faeces.
		18	am	Quiet and huddled.
			pm	Quiet and huddled.
		19	am	Quiet and huddled. Some movement.
			pm	Quiet. More alert.
		20	am	Quiet and huddled. Some movement.
			pm	Quiet and huddled. Some movement.
		21	am	Quiet but alert.
			pm	Quiet but alert.
		22	am	Quiet but alert.
			pm	Quiet but alert.
		23	am	Quiet but alert. Dark faeces.
			pm	Alert and active. Normal faeces.
		24	am	Alert and active.
			pm	Quiet but alert.
		25	am	Quiet.
			pm	Quiet.
		26	am	Quiet but alert. Dark faeces.
			pm	Quiet but alert. Dark faeces.
		27	am	Alert and active. Loose faeces.
			pm	Alert and active. Loose faeces.
		28	am	Quiet but alert. Normal faeces.
			pm	Quiet but alert.
		29	am	Quiet but alert. Occasionally active.
			pm	Quiet but alert. Occasionally active.
		30	am	Quiet but alert. Occasionally active.
			pm	Quiet but alert.
		31	am	Quiet but alert.
			pm	Quiet but alert.
		32	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Normal faeces.
		33	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		34	am	Quiet but alert. Normal faeces.
			pm	Recovering from sedation.
		35	am	Quiet but alert and active.
			pm	Quiet but alert and active.
		36	am	Quiet but alert and active.
			pm	Quiet but alert and active.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
VI (cont)	X51m (cont)	37	am	Quiet but alert.
			pm	Quiet but alert.
		38	am	Quiet but alert. Dark faeces.
			pm	Quiet but alert. Dark faeces.
		39	am	Quiet but alert. Dark faeces.
			pm	Quiet but alert. Dark faeces.
		40	am	Quiet but alert. Dark faeces.
			pm	Alert and active.
		41	am	Alert and active.
			pm	Alert and active.
		42	am	Alert and active.
			pm	Alert and active.
		43	am	Quiet but alert.
			pm	No abnormalities detected.
		44	am	Quiet but alert.
			pm	Quiet but alert.
		45	am	Quiet but alert and active.
			pm	Quiet but alert and active.
		46	am	Comment not recorded.
			pm	No abnormalities detected.
		47	am	Quiet.
			pm	Quiet.
		48	am	Quiet.
			pm	Quiet.
		49	am	Alert and active.
			pm	No abnormalities detected.
		50	am	No abnormalities detected.
			pm	No abnormalities detected.
		51	am	No abnormalities detected.
			pm	No abnormalities detected.
		52	am	Dark faeces.
			pm	Dark faeces.
		53	am	Dark faeces.
			pm	No abnormalities detected.
		54	am	No abnormalities detected.
			pm	No abnormalities detected.
		55	am	No abnormalities detected.
			pm	No abnormalities detected.
		56	am	No abnormalities detected.
			pm	No abnormalities detected.
		57	am	No abnormalities detected. Sacrificed.
	X52f	1	am	Quiet and huddled..
			pm	Quiet and huddled.
		2	am	Quiet and huddled.
			pm	Quiet and huddled.
		3	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
VI (cont)	X52f (cont)	4	am	Quiet and huddled.
			pm	Quiet and huddled.
		5	am	Quiet but alert. Dark faeces.
			pm	Quiet but alert. Dark faeces.
		6	am	Quiet and huddled. Piloerection. Unsteady movement.
			pm	Quiet and huddled. Piloerection. Unsteady movement.
		7	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces. Unsteady movement.
		8	am	Quiet and huddled. Loose/liquid faeces. Unsteady movement.
			pm	Quiet and huddled. Loose/liquid faeces. Unsteady movement.
		9	am	Quiet and huddled. Loose/liquid faeces. Unsteady movement.
			pm	Quiet and huddled. Loose/liquid faeces. Unsteady movement.
		10	am	Quiet and huddled. Loose/liquid faeces. Unsteady movement.
			pm	Quiet and huddled. Loose/liquid faeces. Unsteady movement. Sacrificed.
	X40f	1	am	Quiet and huddled.
			pm	Quiet and huddled.
		2	am	Quiet but alert.
			pm	Quiet but alert.
		3	am	Quiet but alert.
			pm	Quiet but alert.
		4	am	Quiet and huddled. Dark faeces.
			pm	Quiet and huddled. Dark faeces.
		5	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		6	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		7	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		8	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		9	am	Quiet. Loose faeces.
			pm	Liquid faeces.
		10	am	Quiet. Loose/liquid faeces.
			pm	No abnormalities detected.
		11	am	Quiet. Loose faeces.
			pm	Quiet. Loose faeces.
		12	am	Quiet. Loose faeces. Vomit in cage.
			pm	Quiet. Loose faeces. Vomit in cage.
		13	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		14	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		15	am	Quiet but alert. Loose faeces.
			pm	Quiet. Loose faeces.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
VI (cont)	X40f (cont)	16	am	Quiet. Loose faeces.
			pm	Quiet. Loose faeces.
		17	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert.
		18	am	Quiet but alert.
			pm	Quiet and huddled.
		19	am	Quiet but alert.
			pm	Quiet but alert.
		20	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		21	am	Quiet but alert. Loose/liquid faeces.
			pm	Quiet but alert. Loose/liquid faeces.
		22	am	Quiet and huddled. Reluctant to move, unsteady. Liquid faeces.
			pm	Quiet but alert. Occasionally huddled. Liquid faeces.
		23	am	Quiet but alert. Liquid faeces.
			pm	Quiet but alert. Occasionally huddled. Liquid faeces.
		24	am	Quiet but alert. Loose faeces.
			pm	Quiet and huddled.
		25	am	Quiet but alert. Loose/liquid faeces.
			pm	Quiet but alert. Loose/liquid faeces.
		26	am	Quiet but alert. Loose/liquid faeces.
			pm	Quiet but alert. Loose/liquid faeces.
		27	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		28	am	Quiet and huddled. Normal faeces.
			pm	Quiet and huddled.
		29	am	Quiet but alert. Occasionally huddled. Loose faeces.
			pm	Quiet but alert. Occasionally huddled. Loose faeces.
		30	am	Quiet but alert. Slow movement. Occasionally huddled. Normal faeces.
			pm	Quiet but alert.
		31	am	Quiet but alert.
			pm	Quiet but alert.
		32	am	Quiet and huddled but alert.
			pm	Quiet and huddled but alert. Loose faeces.
		33	am	Quiet but alert. Occasionally huddled. Loose faeces.
			pm	Quiet but alert. Occasionally huddled. Loose faeces.
		34	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		35	am	Quiet but alert. Normal faeces.
			pm	Quiet but alert.
		36	am	Quiet but alert and active.
			pm	Quiet but alert.
		37	am	Quiet but alert.
			pm	Quiet but alert.
		38	am	Quiet but alert.
			pm	Quiet but alert.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
VI (cont)	X40f (cont)	39	am	Quiet but alert.
			pm	Quiet but alert.
		40	am	No abnormalities detected.
			pm	Alert and active.
		41	am	Alert and active.
			pm	Alert and active.
		42	am	Alert and active.
			pm	Alert and active.
		43	am	No abnormalities detected.
			pm	No abnormalities detected.
		44	am	No abnormalities detected.
			pm	No abnormalities detected.
		45	am	No abnormalities detected.
			pm	No abnormalities detected.
		46	am	No abnormalities detected.
			pm	No abnormalities detected.
		47	am	No abnormalities detected.
			pm	No abnormalities detected.
		48	am	No abnormalities detected.
			pm	No abnormalities detected.
		49	am	No abnormalities detected.
			pm	No abnormalities detected.
		50	am	No abnormalities detected.
			pm	No abnormalities detected.
		51	am	No abnormalities detected.
			pm	No abnormalities detected.
		52	am	No abnormalities detected.
			pm	Bruise on chin.
		53	am	No abnormalities detected.
			pm	No abnormalities detected.
		54	am	No abnormalities detected.
			pm	No abnormalities detected.
		55	am	No abnormalities detected.
			pm	No abnormalities detected.
		56	am	No abnormalities detected..
			pm	No abnormalities detected.
		57	am	No abnormalities detected. Sacrificed.
	W757m	1	am	Quiet and huddled.
			pm	Quiet and huddled.
		2	am	Quiet but alert.
			pm	Quiet but alert.
		3	am	Quiet but alert.
			pm	Quiet but alert.
		4	am	Quiet and huddled. Dark faeces.
			pm	Quiet and huddled. Dark faeces.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
VI (cont)	W757m (cont)	5	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		6	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		7	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		8	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		9	am	Quiet. Loose faeces.
			pm	Liquid faeces.
		10	am	Quiet. Loose/liquid faeces.
			pm	No abnormalities detected.
		11	am	Quiet. Loose faeces.
			pm	Quiet. Loose faeces.
		12	am	Quiet. Loose faeces. Vomit in cage.
			pm	Quiet. Loose faeces. Vomit in cage.
		13	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		14	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		15	am	Quiet but alert. Loose faeces.
			pm	Quiet. Liquid faeces containing blood.
		16	am	Quiet. Liquid faeces containing blood.
			pm	Quiet. Liquid faeces.
		17	am	Quiet and huddled. Liquid faeces.
			pm	Quiet and huddled. Pale liquid faeces.
		18	am	Quiet and huddled. Liquid faeces.
			pm	Quiet and huddled. Liquid faeces.
		19	am	Quiet and huddled. Reluctant to move. Liquid faeces.
			pm	Quiet and huddled. Reluctant to move. Liquid faeces.
		20	am	Quiet and huddled. Liquid faeces.
			pm	Quiet and huddled. Liquid faeces.
		21	am	Quiet but alert. Loose/liquid faeces.
			pm	Quiet but alert.
		22	am	Quiet but alert. Occasionally huddled. Liquid faeces.
			pm	Quiet but alert. Occasionally huddled. Liquid faeces.
		23	am	Quiet and huddled. Liquid faeces.
			pm	Quiet but alert. Occasionally huddled. Liquid faeces.
		24	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert.
		25	am	Quiet but alert. Loose/liquid faeces.
			pm	Quiet but alert. Loose/liquid faeces.
		26	am	Quiet. Loose/liquid faeces.
			pm	Quiet. Loose/liquid faeces.
		27	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
VI (cont)	W757m (cont)	28	am	Quiet but alert. Pale faeces.
			pm	Quiet but alert.
		29	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		30	am	Quiet but alert. Normal faeces.
			pm	Quiet but alert.
		31	am	Quiet but alert.
			pm	Quiet but alert.
		32	am	Quiet and huddled but alert.
			pm	Quiet and huddled but alert. Loose faeces.
		33	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		34	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		35	am	Quiet but alert. Normal faeces.
			pm	Quiet but alert.
		36	am	Quiet but alert and active.
			pm	Alert and active.
		37	am	Quiet but alert.
			pm	Quiet but alert.
		38	am	Quiet but alert.
			pm	Quiet but alert.
		39	am	Quiet but alert.
			pm	Alert and active.
		40	am	No abnormalities detected.
			pm	Alert and active.
		41	am	Alert and active.
			pm	Alert and active.
		42	am	Alert and active.
			pm	Alert and active.
		43	am	No abnormalities detected.
			pm	No abnormalities detected.
		44	am	No abnormalities detected.
			pm	No abnormalities detected.
		45	am	No abnormalities detected.
			pm	No abnormalities detected.
		46	am	No abnormalities detected.
			pm	No abnormalities detected.
		47	am	No abnormalities detected.
			pm	No abnormalities detected.
		48	am	No abnormalities detected.
			pm	No abnormalities detected.
		49	am	No abnormalities detected.
			pm	No abnormalities detected.
		50	am	No abnormalities detected.
			pm	Sneezing. Blood around both nostrils.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
VI (cont)	W757m (cont)	51	am	Clear discharge around nostrils.
			pm	No abnormalities detected.
		52	am	No abnormalities detected.
			pm	No abnormalities detected.
		53	am	No abnormalities detected.
			pm	No abnormalities detected.
		54	am	No abnormalities detected.
			pm	No abnormalities detected.
		55	am	No abnormalities detected.
			pm	No abnormalities detected.
		56	am	No abnormalities detected.
			pm	No abnormalities detected.
		57	am	No abnormalities detected. Sacrificed.
	W759m	1	am	Quiet and huddled..
			pm	Quiet and huddled.
		2	am	Quiet but alert.
			pm	Quiet but alert.
		3	am	Quiet but alert.
			pm	Quiet but alert.
		4	am	Quiet and huddled. Dark faeces.
			pm	Quiet and huddled. Dark faeces.
		5	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		6	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		7	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		8	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		9	am	Quiet. Loose faeces.
			pm	Liquid faeces.
		10	am	Quiet. Loose/liquid faeces.
			pm	No abnormalities detected.
		11	am	Quiet. Loose faeces.
			pm	Quiet. Loose faeces.
		12	am	Quiet. Loose faeces. Vomit in cage.
			pm	Quiet. Loose faeces. Vomit in cage.
		13	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		14	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		15	am	Quiet but alert. Liquid faeces.
			pm	Quiet.
		16	am	Quiet. Liquid faeces.
			pm	Quiet. Loose/liquid faeces.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
VI (cont)	W759m (cont)	17	am	Quiet and huddled. Liquid faeces.
			pm	Quiet and huddled. Liquid faeces.
		18	am	Quiet and huddled. Liquid faeces.
			pm	Quiet and huddled. Liquid faeces.
		19	am	Quiet and huddled. Liquid faeces. Reluctant to move.
			pm	Quiet and huddled. Liquid faeces. Reluctant to move.
		20	am	Quiet and huddled. Liquid faeces.
			pm	Quiet and huddled. Liquid faeces.
		21	am	Quiet and alert. Loose/liquid faeces. Sacrificed.
	W760f	1	am	Quiet and huddled.
			pm	Quiet and huddled.
		2	am	Quiet but alert.
			pm	Quiet but alert.
		3	am	Quiet but alert.
			pm	Quiet but alert.
		4	am	Quiet and huddled. Dark faeces.
			pm	Quiet and huddled. Dark faeces.
		5	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		6	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		7	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		8	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		9	am	Quiet. Loose faeces.
			pm	Liquid faeces.
		10	am	Quiet. Loose/liquid faeces.
			pm	No abnormalities detected.
		11	am	Quiet. Loose faeces.
			pm	Quiet. Loose faeces.
		12	am	Quiet. Loose faeces. Vomit in cage.
			pm	Quiet. Loose faeces. Vomit in cage.
		13	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		14	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		15	am	Quiet but alert. Loose faeces.
			pm	Quiet. Liquid faeces.
		16	am	Quiet. Liquid faeces.
			pm	Quiet. Liquid faeces.
		17	am	Quiet but alert. Loose faeces.
			pm	Very quiet and huddled.
		18	am	Very quiet and huddled.
			pm	Sacrificed.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
VI (cont)	W458f	1	am	Quiet but alert.
			pm	Quiet but alert.
		2	am	Quiet and huddled.
			pm	Quiet and huddled.
		3	am	Quiet but alert. Dark faeces.
			pm	Quiet but alert. Dark faeces.
		4	am	Quiet and huddled.
			pm	Quiet and huddled.
		5	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		6	am	Quiet and huddled.
			pm	Quiet and huddled.
		7	am	Quiet. Loose/liquid faeces.
			pm	No abnormalities detected.
		8	am	Quiet. Loose/liquid faeces.
			pm	Quiet. Loose/liquid faeces.
		9	am	Quiet. Loose/liquid faeces.
			pm	Quiet. Loose/liquid faeces.
		10	am	Quiet. Loose faeces. Vomit in cage.
			pm	Quiet. Loose faeces. Vomit in cage.
		11	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		12	am	Quiet but alert. Liquid faeces.
			pm	Quiet but alert. Liquid faeces.
		13	am	Quiet but alert. Loose faeces.
			pm	Quiet. Liquid faeces.
		14	am	Quiet. Liquid faeces.
			pm	Quiet and huddled. Liquid faeces.
		15	am	Quiet and huddled. Liquid faeces. Swelling above operation scar.
			pm	Quiet, reluctant to move. Huddled on perch. Slightly unsteady when moving.. Liquid faeces. Swelling above operation scar.
		16	am	Quiet and huddled. Reluctant to move. Unsteady. Liquid faeces. Swelling above operation scar.
			pm	Quiet and huddled. Nasal discharge. Swelling reduced.
		17	am	Quiet and huddled. Reluctant to move. Unsteady. Liquid faeces. Swelling reduced.
			pm	Quiet. Slightly unsteady. Liquid faeces. Swelling reduced.
		18	am	Sacrificed.
	W750f	1	am	Quiet but alert.
			pm	Quiet but alert.
		2	am	Quiet and huddled.
			pm	Quiet and huddled.
		3	am	Quiet but alert. Dark faeces.
			pm	Quiet but alert. Dark faeces.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
VI (cont)	W750f (cont)	4	am	Quiet and huddled.
			pm	Quiet and huddled.
		5	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		6	am	Quiet and huddled.
			pm	Quiet and huddled.
		7	am	Quiet. Loose/liquid faeces.
			pm	No abnormalities detected.
		8	am	Quiet. Loose/liquid faeces.
			pm	Quiet. Loose/liquid faeces.
		9	am	Loose faeces.
			pm	Loose faeces.
		10	am	Quiet. Loose faeces. Vomit in cage.
			pm	Quiet. Loose faeces. Vomit in cage.
		11	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		12	am	Quiet but alert. Liquid faeces.
			pm	Quiet but alert. Liquid faeces.
		13	am	Quiet but alert. Loose faeces.
			pm	Quiet.
		14	am	Quiet. Liquid faeces.
			pm	Quiet. Liquid faeces.
		15	am	Quiet and huddled. Loose faeces.
			pm	Quiet. Reluctant to move. Huddled on perch. Liquid faeces.
		16	am	Quiet and huddled. Liquid faeces.
			pm	Quiet and huddled. Liquid faeces.
		17	am	Quiet and huddled. Reluctant to move. Liquid faeces.
			pm	Quiet and huddled. Reluctant to move. Liquid faeces.
		18	am	Quiet and huddled. Liquid faeces. Dehydrated.
			pm	Quiet and huddled. Liquid faeces.
		19	am	Quiet and huddled. Liquid faeces.
			pm	Quiet and huddled.
		20	am	Quiet and huddled. Liquid faeces.
			pm	Quiet but alert. Occasionally huddled. Liquid faeces. Swelling around eyes.
		21	am	Quiet but alert. Liquid faeces.
			pm	Quiet but alert. Occasionally huddled. Liquid faeces.
		22	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert.
		23	am	Quiet but alert. Loose/liquid faeces.
			pm	Quiet but alert. Loose/liquid faeces.
		24	am	Quiet but alert. Loose/liquid faeces.
			pm	Quiet but alert. Loose/liquid faeces.
		25	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		26	am	Quiet but alert. Pale faeces.
			pm	Quiet but alert. Pale faeces.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
VI (cont)	W750f (cont)	27	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		28	am	Quiet but alert. Occasionally active. Normal faeces.
			pm	Quiet but alert. Occasionally active.
		29	am	Quiet but alert.
			pm	Quiet but alert.
		30	am	Quiet and huddled but alert.
			pm	Quiet and huddled but alert. Loose faeces.
		31	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		32	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		33	am	Quiet but alert. Normal faeces.
			pm	Quiet but alert.
		34	am	Quiet but alert and active.
			pm	Quiet but alert.
		35	am	Quiet but alert.
			pm	Quiet but alert.
		36	am	Quiet but alert.
			pm	Quiet but alert.
		37	am	Quiet but alert.
			pm	Alert and active.
		38	am	No abnormalities detected.
			pm	Alert and active.
		39	am	Alert and active.
			pm	Alert and active.
		40	am	Alert and active.
			pm	Alert and active.
		41	am	No abnormalities detected.
			pm	No abnormalities detected.
		42	am	No abnormalities detected.
			pm	No abnormalities detected.
		43	am	No abnormalities detected.
			pm	No abnormalities detected.
		44	am	No abnormalities detected.
			pm	No abnormalities detected.
		45	am	No abnormalities detected.
			pm	No abnormalities detected.
		46	am	No abnormalities detected.
			pm	No abnormalities detected.
		47	am	No abnormalities detected.
			pm	No abnormalities detected.
		48	am	No abnormalities detected.
			pm	No abnormalities detected.
		49	am	No abnormalities detected.
			pm	No abnormalities detected.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
VI (cont)	W750f (cont)	50	am	No abnormalities detected.
			pm	No abnormalities detected.
		51	am	No abnormalities detected.
			pm	No abnormalities detected.
		52	am	No abnormalities detected.
			pm	No abnormalities detected.
		53	am	No abnormalities detected.
			pm	No abnormalities detected.
		54	am	No abnormalities detected.
			pm	No abnormalities detected.
		55	am	No abnormalities detected. Sacrificed.
	W762f	1	am	Quiet but alert.
			pm	Quiet but alert.
		2	am	Quiet and huddled.
			pm	Quiet and huddled.
		3	am	Quiet but alert. Dark faeces.
			pm	Quiet but alert. Dark faeces.
		4	am	Quiet and huddled.
			pm	Quiet and huddled.
		5	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		6	am	Quiet and huddled.
			pm	Quiet and huddled.
		7	am	Quiet. Loose/liquid faeces.
			pm	No abnormalities detected.
		8	am	Quiet. Loose/liquid faeces.
			pm	Quiet. Loose/liquid faeces.
		9	am	Quiet. Loose faeces.
			pm	Quiet. Loose faeces.
		10	am	Quiet. Loose faeces. Vomit in cage.
			pm	Quiet. Loose faeces. Vomit in cage.
		11	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		12	am	Quiet but alert. Liquid faeces.
			pm	Quiet but alert. Liquid faeces.
		13	am	Quiet but alert. Loose faeces.
			pm	Quiet. Liquid faeces.
		14	am	Quiet. Loose faeces.
			pm	Comment not recorded.
		15	am	Quiet but alert. Liquid faeces.
			pm	Very quiet. Reluctant to move. Huddled on perch. Liquid faeces. Vomit in cage.
		16	am	Quiet and huddled. Liquid faeces. Vomit in cage.
			pm	Quiet and huddled. Liquid faeces. Vomit in cage.
		17	am	Quiet and huddled. Reluctant to move. Liquid faeces.
			pm	Quiet and huddled. Reluctant to move. Liquid faeces.

APPENDIX 8

(Clinical signs - continued)

Phase	Animal no./sex	Day		Clinical signs
VI (cont)	W762f (cont)	18	am	Quiet and huddled. Loose faeces.
			pm	Quiet and huddled. Loose faeces.
		19	am	Found dead in cage – comment in daybook.
	W774f	1	am	Quiet but alert.
			pm	Quiet but alert.
		2	am	Quiet and huddled.
			pm	Quiet and huddled.
		3	am	Quiet but alert. Dark faeces.
			pm	Quiet but alert. Dark faeces.
		4	am	Quiet and huddled.
			pm	Quiet and huddled.
		5	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		6	am	Quiet and huddled.
			pm	Quiet and huddled.
		7	am	Quiet. Loose/liquid faeces.
			pm	No abnormalities detected.
		8	am	Quiet. Loose/liquid faeces.
			pm	Quiet. Loose/liquid faeces.
		9	am	Loose faeces.
			pm	Loose faeces.
		10	am	Quiet. Loose faeces. Vomit in cage.
			pm	Quiet. Loose faeces. Vomit in cage.
		11	am	Quiet but alert. Loose faeces.
			pm	Quiet but alert. Loose faeces.
		12	am	Quiet but alert. Liquid faeces.
			pm	Quiet but alert. Liquid faeces.
		13	am	Quiet but alert. Loose faeces.
			pm	Quiet. Dark/loose faeces.
		14	am	Quiet. Loose faeces.
			pm	Quiet. Loose faeces. Vomit in tray.
		15	am	Quiet but alert. Occasionally huddled. Liquid faeces.
			pm	Quiet and huddled. Liquid faeces.
		16	am	Quiet and huddled. Liquid faeces.
			pm	Quiet and huddled. Liquid faeces.
		17	am	Quiet and huddled. Reluctant to move. Liquid faeces.
			pm	Quiet and huddled. Occasional movement.
		18	am	Found dead in cage.

ITN6: HETEROTOPIC CERVICAL CARDIAC XENOTRANSPLANTATION IN BABOONS

ITN11 is similar.

EXPERIMENTAL PROCEDURE

ANIMAL SUPPLY

Donor animals

Transgenic piglets were selected from litters produced by the Sponsor under Project Licence No. PPL [redacted]. Transgenic piglets supplied for the study were 7 - 21 days old and their weights in the range 2 to 3.5 kg. The Sponsor was responsible for the selection of these animals.

Recipient animals

Wild-caught baboons (*Papio anubis*) originating from Kenya were imported through a UK commercial supplier [redacted]. Their age at the start of the study was estimated to be 2 to 4 years and their weights were in the range 7.8 to 8.5 kg.

The animals used in this study were selected from stock held on behalf of the Sponsor to undergo screening as suitable recipients. Based on the results of the prescreening investigations animals were selected by the Sponsor for transplant (see **PRE-OPERATIVE INVESTIGATIONS**). Only data relating to those animals that underwent transplant is presented in this report.

ANIMAL MANAGEMENT

Piglets

On the day of transplant, selected animals were delivered to Huntingdon Life Sciences by the Sponsor.

Baboons

On arrival at Huntingdon Life Sciences all animals were examined by a Veterinary Officer, received an intramuscular injection of [redacted] to eliminate tapeworm infestation and were allocated a unique colony number, which was tattooed under the right arm. Intrapalpebral tuberculin tests were performed soon after arrival, or at least 6 weeks after the last test performed by the supplier. Due to the frequency of planned laboratory investigations and by virtue of the fact that these animals were immunosuppressed, intrapalpebral tuberculin testing was stopped prior to transplant.

The animals were housed individually in cages specifically designed to house non-human primates in clean and secure conditions. The animals were housed in cages measuring 78 cm wide, 103 cm deep and 230 cm high. The cages were constructed of a stainless steel framework and printboard' walls, shelves and ceiling, incorporating a squeeze-back system, food hopper, water bottle holder and a removable 2.5 × 2.5 cm grid floor. Under the front half of each cage was a removable tray which contained wood chippings (Gold Chips sawdust: [redacted]) for use as a litter/forage substrate. The cages were cleaned and litter replaced each day. Automatic drinking valves, for the supply of drinking water, were used and tested each day.

The room in which the animals were kept was as far as practicable isolated from external disturbances. The room temperature was maintained as far as possible in the range 20 to 26°C, using heat-exchangers connected to hot water supplied from oil-fuelled boilers. Relative humidity was maintained as far as possible in the range 45 to 70%. The environment was governed by a computer controlled building management system which continuously monitored the temperature and humidity controls and the operational state of the air handling plant. Temperature and relative humidity were recorded using a Kent Clearspan recorder. Artificial lighting was used and was controlled to give 12 hours of light and 12 hours of dark per 24 hours. Air extraction was via a balanced system designed to give fifteen air changes per hour.

FOOD AND WATER

Baboons were each offered 350 grams, of standard dry diet (Primate Diet: [redacted] daily. Three hundred and fifty grams were offered in the morning. Prior to commencement of the study Baboon V683 was offered 250 grams of standard dry diet. In the morning, the residue of the previous day was removed and weighed. All animals were starved overnight prior to operation.

Water was available at all times, Vitamin C (Blackcurrant, [redacted]) and [redacted] (a vitamin B_{12} preparation) were added to the drinking water on one day of each week.

There was no information available to the Study Director to indicate that any non-nutrient substance likely to influence the effect of the test substance could reasonably be expected to be present in the diet or the drinking water, both of which are routinely subjected to chemical analysis. Results of all the analyses were lodged in the HRC Archives.

Wholemeal bread and fresh fruit or vegetable produce was sometimes offered in order to enrich the environment and improve the interaction between the animals and their handlers.

STUDY DESIGN

All animals were considered on an individual basis. A total of 3 animals underwent heterotopic cervical cardiac xenotransplantation. The Sponsor was responsible for categorising the reasons why animals were sacrificed (*ie* technical failure, xenograft rejection *etc*).

All animals that underwent transplant received immunosuppressive treatment with a combination of [redacted] immunosuppressive treatment commenced on Day -1; the day of transplant being designated Day 0.

Details of donor-recipient pairings for transplants undertaken and the dates on which they were performed are listed in Appendix 1. All recipient animals were identified by their unique HRC colony number.

The study was designed such that all animals initially followed a standard immunosuppressive protocol prior to and immediately following transplant. After a few days the immunosuppressive regime was then individually tailored for each animal, being based on the results of the laboratory investigations and blood drug levels. The initial dosing regimes are summarised as follows:

The original study required the animals to be dosed orally with [redacted] from Day [redacted] Administration of [redacted] was carried out in this way for the first animal (V683), although the dosage was increased to [redacted] bid by the Sponsor. For the second and third animals (W205 and W201) the commencement and route of administration of [redacted] was changed by the Sponsor. [redacted] was administered by intramuscular injection at a dosage of [redacted] on Day [redacted] following the successful completion of surgery. Thereafter animals received [redacted] orally twice daily, at a dosage specified by the Sponsor. When necessary, dependent on blood [redacted] levels, animals received additional administration of [redacted] by intramuscular injection.

[redacted] was initially administered by intravenous injection on Day [redacted] at a dosage of [redacted] and again on Days [redacted] and [redacted] at a dosage of [redacted]. Subsequently oral administration of [redacted] commenced on Day [redacted] at a dosage of [redacted] and on alternate days thereafter or as required at the discretion of the Sponsor.

[redacted] was administered by intravenous injection at a dosage of [redacted] at the time of transplant (Day [redacted]). Animals were then dosed orally with [redacted] at the same dosage level on Days [redacted] and [redacted] after which the dosage level was reduced daily by [redacted] increments until a dosage of [redacted] was reached. Thereafter any surviving animals were maintained at that dosage level.

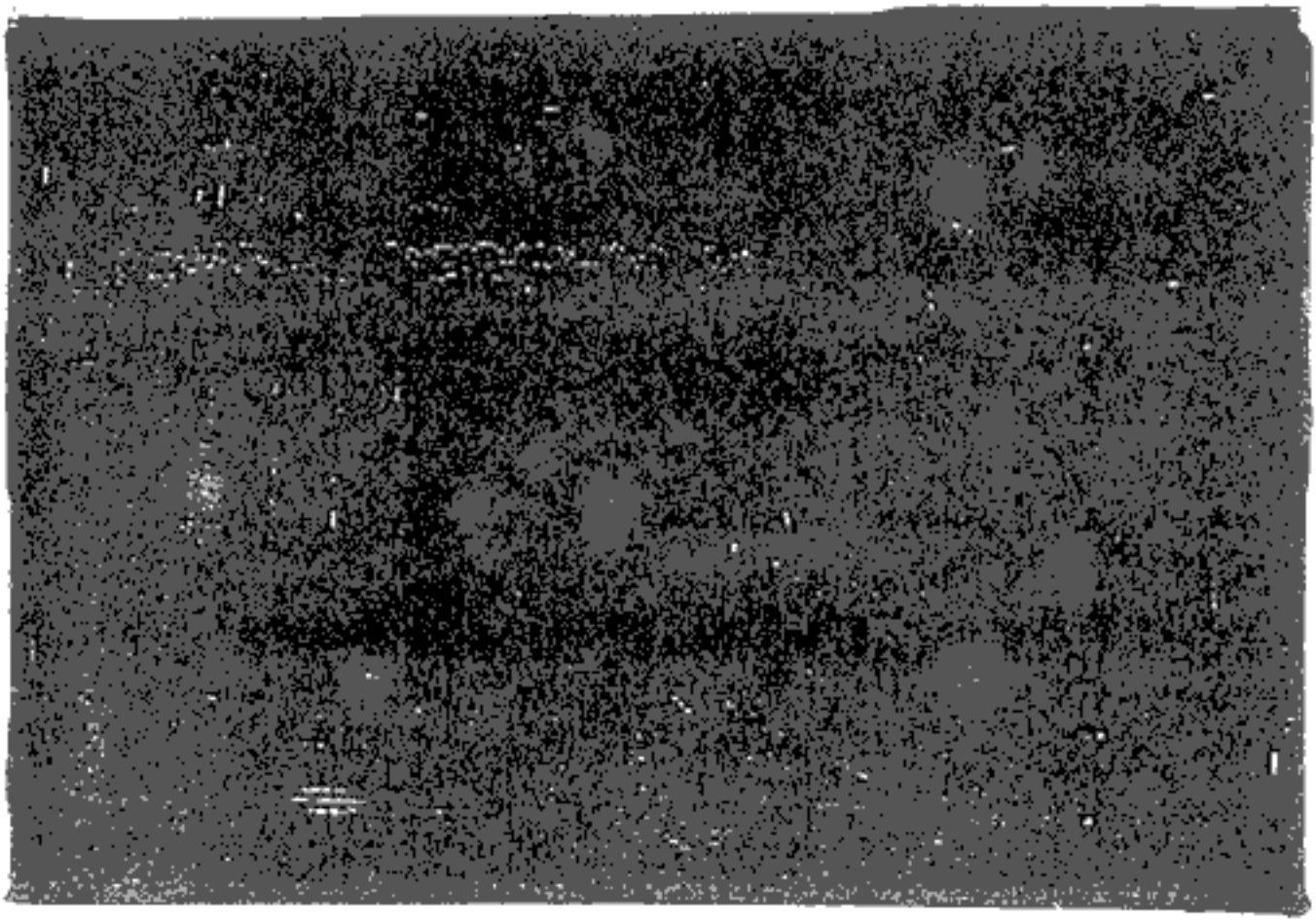
Details of the immunosuppressive regimes applied to individual animals are presented in Appendix 3.

Transplant operations were performed on one recipient animal per day and were spread over a period of several months, dependent on the availability of surgeons. The date of commencement of the study for these animals was therefore different, dependent on when each transplant was performed.

The animals were housed in the [redacted]

PREPARATION OF THE TEST SUBSTANCES

The test substances were prepared for administration as follows:



ADMINISTRATION OF THE TEST SUBSTANCES

The animals were dosed at approximately the same time(s) each day when applicable. Individual doses were adjusted according to the most recent bodyweight. The required quantity of each test solution was measured into a suitably graduated plastic syringe.

For oral dosing, the test solutions were administered through a plastic catheter [redacted] inserted via the mouth into the stomach. The catheter was flushed through with a small quantity (10 ml) of [redacted] (a high carbohydrate, low electrolyte, low fluid drink; [redacted]

For intravenous administration, the test solution was injected using a [redacted] infusion set inserted into the cephalic or saphenous vein.

For intramuscular administration the test solution was injected through an appropriate gauge hypodermic needle. The animal was dosed in the thigh, the hair having been removed by clipping, to facilitate administration and to observe any local reaction to the injection.

Intravenous administration of steroid on the day of transplant was carried out during surgery. The dose was administered through an indwelling cannula inserted into a peripheral vein (ie saphenous).

CHANGES TO TREATMENT REGIMEN/DOSAGE LEVELS

Any changes to the planned treatment regimen, which were made prior to an animal commencing treatment, were detailed by protocol amendment.

Any changes in dosages made after treatment had commenced, arising from the results of laboratory investigations ([redacted] total WBC count, anti-pig antibody level etc) which were considered necessary for the clinical management of individual animals were documented in the study records, but were not detailed by protocol amendment. In this case any changes in dosage levels were only made following written authorisation from either [redacted]

The only exception was that if the total WBC count for any animal fell below $2.0 \times 10^3/mm^3$, HRC could stop administration of [redacted] without any prior authorisation from the Sponsor.

FORMULATION SAMPLING

The pharmaceutical preparations identified in the procedure used in this study were intended for the treatment of animals to prevent the rejection of a transplanted transgenic organ. With the exception of [redacted], these materials were all licensed pharmaceutical products.

Details of batch usage were documented and records of the daily preparation and administration of formulations were maintained. Formulation samples for analysis of achieved concentration were not taken.

PRE-OPERATIVE INVESTIGATIONS

During the acclimatisation period, blood samples were obtained from potential donor animals for various investigations to enable the selection of the most compatible donor-recipient pairings. Blood samples (10 ml into plain tubes), were obtained for the following investigations.

1. Pre-study haematology and biochemistry
2. Anti-pig antibody titres
3. CH50
4. Blood group

Investigations carried out on donor animals were the responsibility of the Sponsor and as such, have been documented and reported separately.

SURGICAL PROCEDURE (including anaesthetic management)

Donor animals

During the preparation of the recipient, the donor animal was sedated with [redacted]. Initial induction of anaesthesia was by inhalation via a face mask and following transfer to the operating table, endotracheal intubation via tracheostomy was performed to allow mechanical ventilation.

The thoracic skin was prepared and draped to expose the operative field and a median sternotomy was performed to expose the intra-thoracic organs. The sternal halves were separated by a retractor, and a thymectomy performed to allow better access to the pericardium, which was opened in the midline. At this stage the pig was heparinised systemically by direct injection of sodium heparin [redacted] into the superior vena cava. Dissection was performed to mobilise the heart and great vessels, passing slings around the intra-pericardial inferior vena cava (IVC), the superior vena cava (SVC), and the ascending aorta. The azygos vein was isolated and divided between ligatures as it entered the posterior aspect of the IVC. At this stage the heart was adequately mobilised for removal.

The ascending aorta was then cross clamped and cold crystalloid cardioplegic solution administered into the aortic route to institute cardioplegic arrest with exsanguination for the animal through the IVC and inferior pulmonary veins which were cut to allow drainage. After arrest was established the heart was excised by dividing in turn the IVC, left inferior and superior pulmonary veins, the left and right pulmonary arteries, the SVC and finally the ascending aorta. The heart was then transferred to a bowl containing cold saline and prepared for implantation. After inspection for a patent foramen ovale, and creation of an atrio-septal defect if one is not present, the IVC and SVC were sutured closed. Next the back wall of the left atrium was prepared and the orifices of the pulmonary veins obliterated.

Recipient animals

All animals were starved overnight prior to surgery. Prior to transfer to the operating theatre the animals were sedated with [redacted] given by the intramuscular route in combination with [redacted]).

Following induction of anaesthesia by intravenous injection of [redacted] an endotracheal tube was inserted and the animals were maintained on a [redacted] mixture, with the addition of [redacted] at a concentration of [redacted] as required.

Prophylactic antibiotic therapy was given [redacted].

An indwelling cannula was inserted into a peripheral vein for administration of fluids and drugs etc during the procedure. The animal was transferred to the operating table where appropriate respiratory and electrocardiographic monitoring was established.

Cervical heterotopic heart implantation was performed by inserting the heart from the donor animal into a subcutaneous pocket previously fashioned to accommodate it. Vascular connections were made as follows:

Donor heart		Recipient
Aorta	→	Carotid artery
Pulmonary artery	→	Jugular vein

Connection of the donor and recipient blood vessels was by end to side anastomoses. On completion of the anastomoses the carotid and jugular clamps were removed and the implanted heart observed until stable rhythm was observed and haemostasis achieved.

Once the surgeon was satisfied that there was stable xenograft function and adequate haemostasis was observed the surgical site was closed and the recipient allowed to recover from general anaesthesia. The animal was then returned to its cage.

POST-OPERATIVE MANAGEMENT

Recipient animals were closely monitored for the first 24 hours post-operation. Heat lamps and/or thermostatic electric fan heaters were used to keep the animals warm until such time their use was no longer required, as determined by the attending veterinarian.

Post-operative analgesia was provided by the use of [redacted] which was administered at the discretion of the attending veterinary surgeon. Other drugs were also prescribed if considered appropriate. Details of individual drug administrations were recorded in the study records.

Animals received two subcutaneous administrations of [redacted] on the day prior to transplant. From Day 0, a single dose was given daily (or more frequently if considered necessary) at the discretion of the attending veterinarian. Animals received a subcutaneous dose at a dosage of [redacted]

Dependent on the clinical condition of each animal, food and/or fluid supplements may have been given at the discretion of the attending veterinary surgeon and/or Sponsor's monitoring scientist (or their deputy).

In the event of any animal showing a deterioration in it's clinical condition, heat lamps were used at the discretion of the attending HRC veterinarian.

POST-OPERATIVE OBSERVATIONS

Dated and signed records of all activities relating to the day by day running and maintenance of the study within the animal unit, as well as to the observations and examinations outlined in this protocol, were recorded in the Study Day Book. In addition, observations relating to individual animals made throughout the day were recorded.

The following observations were made during the course of the study:

Mortality

The circumstances of any death was recorded in detail and a full *post mortem* examination was performed as described later. Prior to death, observations listed in this protocol were carried out, where practicable.

Clinical signs

All signs of ill health or reaction to treatment was recorded. Animals were checked regularly throughout the working day from approximately 0830 to 1700 hours (including weekends).

The animals were removed from their cages at regular intervals to assess their general condition and to palpate the transplanted heart to check for cardiac activity (see POST-OPERATIVE INVESTIGATIONS).

Bodyweight

The bodyweight of all animals was recorded generally weekly during the pre-operative period and daily during the post-operative period. The animals were weighed in the morning prior to dosing, or at a similar time during the pre-dosing period.

Food consumption

The quantity of food (standard dry diet) left by individual animals together with an estimate of the quantity spilled was recorded on a daily basis throughout the experimental period. From these data the quantities consumed were calculated.

POST-OPERATIVE INVESTIGATIONS

Xenograft function and physical examination

The functioning of the xenograft was determined at least three times each day (approximately 0900, 1600 and 2100) for the first 2 weeks following transplant and then at least twice daily (approximately 0900 and 1700). Thereafter xenograft function was checked more frequently at the discretion of the Study Director and/or HRC veterinary staff. A check of the general physical condition of the animal was also performed at the same time.

If it was not possible to observe the xenograft functioning whilst the animal was in its cage, the animal was removed from its cage and the xenograft palpated, if necessary.

At these occasions additional treatments *ie* topical applications to wound, analgesics etc, may have been given to the animal as prescribed or directed by HRC's veterinarian or the Sponsor's representatives.

Blood sampling

Blood samples were obtained on Monday, Wednesday and Friday throughout the post-operative period. Blood samples were taken in the morning prior to any dosing. For individual animals, the frequency of the various investigations and the parameters measured were occasionally amended at the Sponsor's request on the basis of the animal's clinical condition or previous results.

(a) Laboratory investigations performed at Huntingdon Life Sciences

Haematology and biochemistry investigations performed as follows:

Haematology	Units
300 µl into 0.5 ml EDTA tube. The following investigations were performed with a Bayer-Technicon H1E haematology analyser:	
Packed cell volume (PCV)	%
Haemoglobin (Hb)	g/dl
Red blood cell count (RBC)	$\times 10^{12}/l$
Total white cell count (WBC Total)	$\times 10^{9}/l$
Platelet count (Plts)	$\times 10^{9}/l$

		Units
Differential WBC count		
Neutrophils	(N)	
Lymphocytes	(L)	
Eosinophils	(E)	$\times 10^9/l$
Basophils	(B)	
Monocytes	(M)	
Large unstained cells	(LUC)	

Cell Morphology : If definitely abnormal cells were observed when examining any stained slide, such as the presence of Heinz bodies or abnormal lymphocytes etc, their presence or absence on each such slide examined was recorded and tabulated separately.

Biochemistry

700 µl into heparinised microtainer. The following parameters were analysed with a Hitachi 737 Clinical Chemistry analyser:

Creatinine	mg/dl
Sodium (Na)	mEq/l
Potassium (K)	mEq/l
Calcium (Ca)	mEq/l
Inorganic Phosphorus (P)	mEq/l
Chloride (Cl)	mEq/l

(b) **Blood samples for analyses by Sponsor or other laboratory**

Anti-pig antibody levels

0.5 ml into plain tube. Samples were analysed at [redacted]

[redacted]

0.2 ml into 0.5 ml EDTA tube. Samples were analysed at [redacted]

The results of these investigations were used to adjust the dosage of the various immunosuppressive treatments as required. The results of the investigations performed at HRC are presented in this report.

TERMINAL STUDIES

The animals were maintained and dosed according to the immunosuppressive protocol unless sacrifice was required due to one of the following events occurring.

1. rejection of xenograft, as defined by absence of palpable cardiac activity.

2. opportunistic infection, as a result of the immunosuppressive treatment. Any signs of infection were brought to the attention of HRC veterinary staff and was treated symptomatically as considered necessary. In the event of an animal developing an infection that could not be treated, the animal was sacrificed following authorisation by the attending veterinarian.

3. drug toxicity, arising from the immunosuppressive treatment. Regular monitoring of the animals both clinically and by blood sampling minimised the risk of drug toxicity.

4. wound breakdown.

The Sponsor was contacted before any decision was taken to sacrifice an animal.

Pre-terminal blood sampling

Prior to sacrifice as much blood as practicable was collected and divided appropriately into heparinised and plain blood tubes.

Following centrifugation the plasma/serum was separated and deep frozen (in cardice) prior to despatch to the Sponsor for analysis.

Necropsy procedure

Each animal was immobilised with [redacted] given by the intramuscular route. The animals were then killed by a lethal dose of [redacted] and then rapidly exsanguinated by incision of the carotid blood vessels.

Immediately after exsanguination the xenograft with its associated anastomoses was carefully removed and weighed. A small section from the wall of each of the four chambers was taken and placed on a cork disc, covered in OCT-embedding matrix [redacted] and rapidly frozen in liquid nitrogen. Each section was then individually wrapped in foil and stored deep frozen in cardice, prior to despatch to the Sponsor. In addition, two pieces were collected into cryovials, frozen in liquid nitrogen and stored deep frozen in cardice.

The remainder of the heart, with the exception of samples for virus studies (see below), was placed in neutral-buffered formalin.

Virus studies

Samples of the following tissues were required from all recipient animals where the cardiac xenograft had survived in excess of 5 days. The size of the sample was ideally approximately 0.5 cm^3 or if this size was not possible, as much was feasible.

- transplanted heart
- vascular anastomoses (junction or donor pulmonary artery and aorta and recipient jugular vein/carotid artery
- lining of abdominal cavity that had been in contact with the transplanted heart
- kidney
- heart (recipient)
- lung
- liver
- testes
- pancreas
- brain
- ileum
- mid-colon

For individual animals other tissue samples were taken at the discretion of the Sponsor's Monitoring Scientist and documented in the study records.

All samples were snap frozen in liquid nitrogen and stored deep frozen (in cardice) prior to despatch to the Sponsor.

ARCHIVING

All raw data, samples and specimens arising from the performance of this study will remain the property of the Sponsor.

All specimens sent to the Sponsor or other Sponsor-nominated laboratory are the responsibility of the Sponsor in respect of storage and archiving. Data and other records arising from any investigations performed on these specimens will be retained and archived by the Sponsor.

All other samples and specimens and all other raw data will be retained by Huntingdon Life Sciences in its archive for a period of five years from the date on which the Study Director signs the final report. After such time, the Sponsor will be contacted and his advice sought on the return, disposal or further retention of the materials. If requested, Huntingdon Life Sciences will continue to retain the materials subject to a reasonable fee being agreed with the Sponsor.

Huntingdon Life Sciences will retain the Quality Assurance records relevant to this study and a copy of the final report in its archive indefinately.

PROCEDURES

The procedures used during the study at Huntingdon, with the exception of the anaesthesia and surgical procedures, were documented in the relevant Huntingdon Life Sciences Procedures Manuals.

DEVIATIONS FROM PROTOCOL

There were no other deviations from protocol other than those documented as File Notes or in the study records and which related to the clinical management of individual animals on a day-to-day basis.

APPENDIX 9

Clinical signs

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1).

3. Missing observations - animal not returned from theatre or recovering from sedation.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
V683m	1	am	Quiet but alert, occasionally huddled. Pale.
		pm	Quiet, unusual posture, no movement.
	2	am	Quiet but alert. No movement. Loose faeces. Neck slightly swollen and bruised.
		pm	Quiet and huddled, occasionally active. Loose faeces. Neck slightly swollen and bruised.
	3	am	Quiet and huddled. Slow movement. Appears thin. Generalised swelling around implanted heart, slight haematoma.
		pm	Quiet and huddled. Slow movement. Small volume of red fluid aspirated from site of transplant.
	4	am	Quiet and huddled, subdued but marginally brighter. No movement. Loose faeces
		pm	Quiet and huddled. No movement. Loose faeces. . Neck still swollen.
	5	am	Quiet and huddled. Minimal movement. Loose faeces.
		pm	Quiet and huddled. Minimal movement. Loose faeces.
	6	am	Quiet and huddled. Small amount of movement. Loose faeces.
		pm	Alert. Some activity on perch. Bright appearance.
	7	am	Quiet and huddled. Normal faeces.
		pm	Quiet and huddled.
	8	am	Quiet but alert. Dried blood around both nostrils.
		pm	Quiet but alert.
	9	am	Quiet but alert. Loose faeces.
		pm	Quiet but alert. Loose faeces.
	10	am	Quiet but alert. Normal faeces.
		pm	Quiet but alert.
	11	am	Quiet but alert.
		pm	Quiet but alert.
	12	am	Quiet but alert.
		pm	Quiet but alert.
	13	am	Quiet but alert. Loose faeces.
		pm	Quiet but alert. Normal faeces. Transplanted heart noted to be slow and decreased vigour of contraction (17.00). Heart completely stopped (21.00). Sacrificed.
W205m	1	am	Active and alert.
		pm	Quiet. No other abnormalities detected.
	2	am	Quiet but alert. Transplanted heart possibly fibrillating.
		pm	Quiet but alert. Transplanted heart beating normally.
	3	am	Quiet but alert. Transplanted heart beating well.
		pm	Quiet but alert.
	4	am	Quiet but alert.
		pm	Quiet but alert. Neck swollen. Transplanted heart beating satisfactorily.
	5	am	Quiet but alert. Vomit on cage floor.
		pm	Quiet but alert.
	6	am	Quiet but alert.
		pm	Quiet but alert.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
W205m (contd)	7	am	Quiet but alert.
		pm	Quiet but alert.
	8	am	Quiet but alert. Heart beating satisfactorily.
		pm	Quiet but alert.
	9	am	Quiet but alert. Vomit in cage.
		pm	Quiet but alert.
	10	am	Quiet but alert.
		pm	Quiet but alert.
	11	am	Quiet but alert. Occasionally huddled.
		pm	Quiet and huddled. Transplanted heart seems very large and possibly discomforting animal. Neck swollen.
	12	am	Quiet and huddled. Holding neck. Appears unsteady.
		pm	Quiet and huddled. Holding neck. Appears unsteady.
	13	am	Quiet and huddled. Holding neck. Appears unsteady.
		pm	Quiet and huddled. Supporting neck with left arm. Unsteady when moving.
	14	am	Quiet and huddled. Transplanted heart swollen and red, seeping yellow fluid.
		pm	Quiet and huddled. Transplanted heart swollen and red, seeping yellow fluid.
	15	am	Quiet and huddled. Transplanted heart appears swollen. Yellow fluid around swelling.
		pm	Quiet and huddled. Transplanted heart appears swollen. Yellow fluid around swelling.
	16	am	Quiet and huddled. Transplanted heart appears swollen. Animal picking at transplant site. Yellow fluid around swelling.
		pm	Quiet and huddled. Transplanted heart appears swollen. Animal picking at transplant site. Yellow fluid around swelling.
	17	am	Quiet and huddled. Swollen around site of transplanted heart. Yellow fluid around wound, feels warm to the touch.
		pm	Quiet and huddled. Swollen around site of transplanted heart. Yellow fluid around wound, feels warm to the touch. Approximately 12 ml of purulent fluid aspirated.
	18	am	Quiet and huddled. Swollen around site of transplanted heart. Yellow fluid seeping from site, also some dry scabs.
		pm	Quiet and huddled. Swollen around site of transplanted heart. Yellow fluid seeping from site, also some dry scabs.
	19	am	Quiet and huddled. Scar on neck appears dry.
		pm	Quiet and alert.
	20	am	Quiet but alert. Scab on operation site appears clean and dry. Keeps holding area where transplanted heart is.
		pm	Quiet and huddled. Little movement and unsteady when moving. Showing signs of discomfort.
	21	am	Quiet and huddled. Scab on operation site appears dry. Reluctant to move. Marked firm swelling around implant. Animal showing obvious discomfort. Fluid swelling developing in sub-mandibular region.
		pm	Sero-sanguinous fluid drained but no purulent material. Transplanted heart beat barely palpable. Swelling so large animal sacrificed for humane reasons.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W201m	1 am	Quiet and huddled. Reluctant to use left leg. Transplanted heart beat just palpable.
	pm	Quiet, sitting on cage floor. Transplanted heart beat very faint and swelling in neck still considerable. Some seepage of blood from wound (17.20). Lying on cage floor, uncoordinated limb spasms for approximately 30 seconds, then sits up and appears alert and normal again (22.45).
	2 am	Very quiet, with limited use of left side. Sacrificed for humane reasons.

ITN8: BONE XENOTRANSPLANTATION IN CYNOLMOLGUS MONKEYS

ITN15 is similar.

EXPERIMENTAL PROCEDURE

ANIMAL SUPPLY

A total of 12 (6 male and 6 female) captive-bred cynomolgus monkeys (*Macaca fascicularis*) were allocated to the study from stock held at Huntingdon. The animals were bred at [redacted] and were imported through a UK commercial supplier [redacted]. The age of the animals at allocation to the study was 2 - 3 years and their weights were in the range 2.7 to 3.3 kg.

ANIMAL MANAGEMENT

Cynomolgus monkeys

All animals were conditioned in England for at least 4 weeks before delivery to the Huntingdon Life Sciences. Documentation received from the supplier included details relating to quarantine dates, health screening and any treatment administered during the conditioning period. On arrival at Huntingdon Life Sciences they were examined by a Veterinary Officer and allocated a unique colony number, which was tattooed under the right arm. Intrapalpebral tuberculin tests were performed at intervals of approximately 8 weeks, beginning prior to and soon after arrival. For transplanted animals, due to the frequency of planned laboratory investigations and due to the nature of the study, intrapalpebral tuberculin testing was stopped following transplant.

The animals were initially housed individually in cages specifically designed to house non-human primates in clean and secure conditions. The animals were housed in cages measuring 73 cm wide, 82 cm deep and 100 cm high. The cages were constructed of aluminium and electro-polished stainless steel, incorporating a squeeze-back system, food hopper, bottle holder and a 2.5 × 2.5 cm grid floor. The cages were changed during the study. The cages were entirely wall-mounted in two tiers, each tier combined with an excreta removal flushing system which was cleaned twice daily after recording food residues. Automatic drinking valves, for the supply of drinking water, were used and tested each day.

From 23 April 1996 the animals were housed in pairs in cages specifically designed to house non-human primates in clean and secure conditions. The animals were housed in cages measuring 78 cm wide, 103 cm deep and 230 cm high. The cages were constructed of a stainless steel framework and printboard walls, shelves and ceiling, incorporating a squeeze-back system, food hopper, water bottle holder and a removable 2.5 × 2.5 cm grid floor. Under the front half of each cage was a removable tray which contained wood chippings (Gold Chips sawdust: [redacted]) for use as a litter/forage substrate. The cages were cleaned and litter replaced each day after recording any food residues. Automatic drinking valves, for the supply of drinking water, were used and were fitted in both upper and lower parts of the cages.

The rooms in which the animals were kept was as far as practicable isolated from external disturbances. Room temperature was maintained in the range 16 to 24°C, using heat exchangers connected to hot water supplied from oil-fuelled boilers. Relative humidity was maintained in the range 38 to 86%. The environment was governed by a computer controlled building management system which continuously monitored the temperature and humidity controls and the operational state of the air handling plant. Temperature and relative humidity were recorded using a Kent Clearspan Recorder. Deviations in temperature and/or relative humidity outside the set limits (20 - 26°C, 45 – 70% RH) were due to the use of fan heaters as supplementary heat sources and when water was used to wash down cages and/or floors and were not considered to impact upon the study. Artificial lighting was used and was controlled to give 12 hours of light and 12 hours of dark per 24 hours. Air extraction was via a balanced system designed to give fifteen air changes per hour.

FOOD AND WATER

Cynomolgus monkeys were each offered 200 grams, of standard dry diet (Primate Diet: [redacted], daily. One hundred grams were offered in the morning and the second 100 grams in the afternoon. From 24 April 1996 they were offered 150 grams in the morning. In the morning, the residue of the previous day was removed and weighed. All animals were starved overnight prior to operation.

Water was available at all times, Vitamin C (Blackcurrant, [redacted] and [redacted] a vitamin B_{12} preparation, [redacted] were added to the drinking water on one day of each week.

There was no information available to the Study Director to indicate that any non-nutrient substance likely to influence the effect of the test substance could reasonably be expected to be present in the diet or the drinking water, both of which are routinely subjected to chemical analysis. Results of all the analyses were lodged in the Huntingdon Life Sciences Archives (Huntingdon).

Wholemeal bread and fresh fruit or vegetable produce was offered in order to enrich the environment and improve the interaction between the animals and their handlers.

STUDY DESIGN

The monkeys allocated to the study received grafts of morselised bone from either transgenic (hDAF +ve) or control (hDAF -ve) pigs. A total of 12 animals (6 males and 6 females) therefore received either transgenic or control xenografts.

For blinding purposes, the morselised bone used for each transplant was identified by number only and randomly allocated for grafting. The allocation of individual animals to each group (hDAF +ve) or (hDAF -ve) could therefore not be specified.

Transplants were performed on 4 animals per day and was spread over a period of 5 weeks dependent on the availability of the surgeon. The commencement of the study for these sub-groups, therefore, varied dependent on when the transplant was performed.

Animals were identified by their colony number. The identities of the animals allocated to each sub-group were as follows:

Sub-group	Animal nos.
1	W15m, W17m, W16f, W22f
2	W25m, W31m, W30f, W36f
3	W45m, W139m, W42f, W280f

The animals were housed in the [redacted]
From 23 April 1996 the animals were housed in the [redacted] for the remainder of the study.

PRE-OPERATIVE INVESTIGATIONS

On Day –4 or on the day of transplant, prior to surgery, blood samples were obtained from animals for the following investigations:

1. Anti-pig antibody titres
2. Routine haematological and biochemical investigations

See POST-OPERATIVE INVESTIGATIONS for the type of sample and investigations performed.

SURGICAL PROCEDURE (including anaesthetic management)

The day of transplant was designated Day 0.

All animals were starved overnight prior to surgery. Prior to transfer to the operating theatre the animal was sedated with [redacted]) given by the intramuscular route in combination with [redacted] injection, [redacted]).

Following induction of anaesthesia by intravenous injection of [redacted] an endotracheal tube was inserted and the animals were maintained on a [redacted] mixture, with the addition of [redacted] at a concentration of [redacted] as required.

Prophylactic antibiotic therapy, either [redacted] or [redacted], was given by subcutaneous injection on Day 0 and for 3 further days afterwards.

An indwelling cannula was inserted into a peripheral vein for administration of fluids and drugs during the procedure. The animal was transferred to the operating table where appropriate respiratory and electrocardiographic monitoring was established.

The dorsum of the base of the tail was shaved.

A midline incision was made longitudinally at the base of the tail down to bone and the 2nd and 3rd caudal vertebrae were exposed by sharp and blunt dissection. The dorsal cortex was removed from both vertebrae and the cancellous core was extracted. The cavity thus created in one vertebra was filled with impacted xenograft, but in the other it was left unfilled. Haemostasis was achieved with diathermy, and the wound was closed with 3/0 undyed vicryl sutures to the muscle and skin. Subcuticular sutures were used to close the skin.

The tail was not docked unless considered necessary by the surgeon.

POST-OPERATIVE MANAGEMENT

Recipient animals were closely monitored until fully recovered from the operation.

Post-operative analgesia was provided by the use of [redacted] which was administered at the discretion of the attending veterinary surgeon. Other drugs may have been prescribed if considered appropriate. Details of individual drug administrations were recorded in the study records.

Dependent on the clinical condition of each animal, food and/or fluid supplements were given at the discretion of the attending veterinary surgeon and/or Sponsor's monitoring scientist (or their deputy). Details of any food and/or fluid supplements which were given to animals were recorded in the study records.

POST-OPERATIVE OBSERVATIONS

Dated and signed records of all activities relating to the day by day running and maintenance of the study within the animal unit, as well as to the group observations and examinations outlined in this protocol, were recorded in the Study Day Book. In addition, observations relating to individual animals made throughout the day were recorded.

The following observations were made during the course of the study:

Clinical signs

All signs of ill health or reaction to treatment were recorded. Animals were checked regularly throughout the working day from approximately 0800 to 1700 hours (including weekends and public holidays).The animals were removed from their cages at least once a day to examine the condition of the wound and apply any treatments if necessary.

Bodyweight

The bodyweight of all animals were generally recorded weekly throughout the duration of the study.

Food consumption

The quantity of food (standard dry diet) left by each individual or pair of animals together with an estimate of the quantity spilled was recorded on a daily basis throughout the experimental period. From these data the quantities consumed were calculated.

POST-OPERATIVE INVESTIGATIONS

Blood sampling

Blood samples were obtained on Mondays, Wednesdays and Fridays throughout the post-operative period. Blood samples were taken in the morning prior to any dosing for the following investigations:

(a) **Laboratory investigations performed at Huntingdon Life Sciences (Huntingdon)**

Haematology and biochemistry investigations were performed on one day each week (Wednesday). The following investigations were performed:

Haematology	**Units**
300 µl into 0.5 ml EDTA tube. The following investigations were performed using a Bayer-Technicon H1E haematology analyser:	
Packed cell volume (PCV)	%
Haemoglobin (Hb)	g/dl
Red blood cell count (RBC)	$\times 10^{12}/l$
Total white cell count (WBC Total)	$\times 10^{9}/l$
Platelet count (Plts)	$\times 10^{9}/l$

Units

Differential WBC count

Neutrophils	(N)	
Lymphocytes	(L)	
Eosinophils	(E)	$\times 10^9/l$
Basophils	(B)	
Monocytes	(M)	

Cell Morphology : the most common morphological changes (anisocytosis, micro/macrocytosis, variation in colour, hypo/hyperchromasia, left shift, atypical/blast cells) were recorded as follows:

\- = No abnormalities detected
\+ = slight
++ = moderate
+++ = marked

In the case of atypical/blast cells, or other abnormalities, confirmation or a written description from a blood film was made.

Biochemistry

700 µl into heparinised microtainer. The following parameters were analysed with a Hitachi 737 Clinical Chemistry analyser

* Total protein	g/dl
* Urea	mg/dl
Creatinine	mg/dl
Sodium (Na)	mEq/l
Potassium (K)	mEq/l
Calcium (Ca)	mEq/l
Inorganic Phosphorus (P)	mEq/l
Chloride (Cl)	mEq/l

The following parameter was analysed as follows:

* Osmolality (Osmol) - using a Wescot vapour-pressure osmometer	mOsm/kg

* These parameters were only investigated for individual animals as recommended by the Sponsor

(b) **Blood samples for despatch to [redacted] or [redacted]**

Anti-pig antibody levels (Serum)

0.5 ml into plain microtainer. Samples were analysed at [redacted] for anti-pig antibody levels.

The blood samples were obtained in the morning. On Mondays, Wednesdays and Fridays samples for [redacted] were despatched so as to arrive no later than 11.00 am.

BIOPSY

Biopsies of the grafted and non-grafted vertebrae were performed on or around Days 7, 30 and 60 after transplant, for all animals. The actual days on which the biopsies were performed for each sub-group of animals was as follows:

Sub-group	Animal numbers	Days of biopsy
1	W15m, W17m, W16f, W22f	8, 35, 63
2	W25m, W31m, W30f, W36f	5, 34, 63
3	W45m, W139m, W42f, W280f	7, 36, 59

Before each biopsy, the animals received an intravenous injection of a fluorochrome to label the bone as follows:

The schedule for the administration of the fluorochrome labels and the subsequent biopsies for each sub-group was as follows:

Date (1996)	Sub-group 1 (T = 27.2.96	Sub-group 2 (T = 6.3.96)	Sub-group 3 (T = 2.4.96)
6 March	Biopsy (D8)		
11March		Biopsy (D5)	
19 March	Xylenol		
20 March	Xylenol		
26 March		Xylenol	
27 March		Xylenol	
28 March	Xylenol		
29 March	Xylenol		
2 April	Biopsy (D35)		
4 April		Xylenol	
5 April		Xylenol	
9 April		Biopsy (D34)	Biopsy (D7)
17 April	Calcein		
18 April	Calcein		
23 April		Calcein	Xylenol
24 April		Calcein	Xylenol
26 April	Calcein		
27 April	Calcein		
30 April	Biopsy (D63)		
2 May		Calcein	Xylenol
3 May		Calcein	Xylenol
8 May		Biopsy (63)	Biopsy (D36)
14 May	[redacted]		
15 May			
21 May		[redacted]	Calcein
22 May	[redacted]		Calcein
23 May			
24 May			
28 May	Kill		
30 May		[redacted]	Calcein x2
31 May			Biopsy (D59)
4 June		Kill	
25 June			[redacted]
26 June			
4 July			
5 July			
8 July			Kill

T Date of transplant
D Day

[redacted]

Animals received intravenous injections of fluorochrome prior to biopsy as follows:

'Day 30' biopsy - xylenol orange (90 mg/kg)

'Day 60' biopsy - calcein (30 mg/kg)

Pre-terminal biopsy - [redacted]

The fluorochrome labels were formulated and administered as follows:

Xylenol orange - a solution was prepared in normal saline at a concentration of 90 mg/ml. The solution was administered at a dosage volume of 1 ml/kg bodyweight.

Calcein - a solution was prepared in 0.2% sodium bicarbonate in normal saline at a concentration of 6 mg/ml. The solution was administered at a dosage volume of 5 ml/kg bodyweight.

[redacted] a solution was prepared in normal saline at a concentration of [redacted] The solution was administered at a dosage volume of [redacted] bodyweight.

The dosing solutions were administered by slow intravenous injection (*ca* 3 - 5 ml/min) into the saphenous or cephalic vein *via* a [redacted] infusion set. Individual doses were calculated based on the most recent bodyweight.

On the day of biopsy the animals were sedated using [redacted] given by the intramuscular route at an appropriate dosage. Additional anaesthesia was provided with a [redacted] mixture, with the addition of [redacted] at a concentration of [redacted] as required.

Immediately prior to the biopsy procedure, x-ray radiographs of the tail were taken in two planes (ventro-dorsal and lateral). For the biopsy procedure, a 16G sterile needle was passed through the lateral skin and lateral cortex into the body of each vertebra. The biopsy needle was withdrawn and the biopsy sample placed in hexane freezing mixture (industrial methylated spirits and cardice) subsequent to being taken by the Sponsor. Light pressure was applied to the tail until any bleeding had stopped.

Appropriate analgesia, as prescribed by the attending veterinary officer, was given to cover the post-biopsy period.

TERMINAL STUDIES

The animals were maintained nominally for 90 days following transplant after which they were sacrificed.

Pre-terminal blood sampling

Prior to sacrifice as much blood as practicable was collected and divided appropriately into heparinised and plain blood tubes.

Following centrifugation the plasma/serum was separated and stored deep frozen in cardice prior to despatch to the Sponsor for analysis.

Necropsy procedure

Each animal was immobilised with [redacted] given by the intramuscular route. The animals were then killed by a lethal dose of [redacted] and then rapidly exsanguinated by incision of the carotid blood vessels.

Immediately after exsanguination the whole tail was carefully removed. The tail was frozen in liquid nitrogen and stored deep frozen in cardice prior to despatch to the Sponsor for examination.

Virus studies

Samples of the following tissues were taken, in triplicate, from all recipient animals. The size of the sample was ideally approximately 0.5 cm^3 or if this size was not possible, as much was feasible.

- brain
- heart
- ileum
- kidney
- liver
- lung
- mesenteric lymph node
- mid-colon
- ovaries or testes
- pancreas
- retro-peritoneal lymph node
- spleen
- sternum

All samples were snap frozen in liquid nitrogen and stored in cardice prior to despatch to the Sponsor

LOCATION OF STUDY RECORDS

All raw data, samples and specimens arising from the performance of this study will remain the property of the Sponsor.

All specimens sent to the Sponsor or other Sponsor-nominated laboratory are the responsibility of the Sponsor in respect of storage and archiving. Data and other records arising from any investigations performed on these specimens will be retained and archived by the Sponsor.

Any other samples and specimens and all other raw data will be retained by Huntingdon Life Sciences in its archive for a period of five years from the date on which the Study Director signs the final report. After such time, the Sponsor will be contacted and his advice sought on the return, disposal or further retention of the materials. If requested, Huntingdon Life Sciences will continue to retain the materials subject to a reasonable fee being agree with the Sponsor.

Huntingdon Life Sciences will retain the Quality Assurance records relevant to this study and a copy of the final report in its archive indefinately.

PROCEDURES

The procedures used during the study, with the exception of the anaesthesia, radiography, biopsy and surgical procedures, were documented in the relevant Huntingdon Life Sciences Procedures Manuals.

DEVIATIONS FROM PROTOCOL

There were no other deviations from protocol other than those documented as File Notes or in the study records.

APPENDIX 6

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1).

3. The observation(s) of purple discolouration of skin, tongue, gums and/or urine was associated with the administration of the fluorochrome dye, xylenol orange, administered prior to biopsy (*ca* Day 30). As such these signs were not considered to be a reaction to treatment, rather a passive consequence.

Abbreviations

Nad No abnormalities detected

APPENDIX 6

Clinical signs

Animal no./sex	Day no.	Clinical signs
W15m	1 am	Nad
	pm	Nad
	1 am	Loose faeces.
	pm	Nad
	2 am	Loose faeces.
	pm	Loose faeces.
	3 am	Loose faeces.
	pm	Loose faeces.
	4 am	Loose faeces.
	pm	Liquid faeces.
	5 am	Liquid faeces.
	pm	Liquid faeces.
	6 am	Normal faeces.
	pm	Nad
	7 am	Nad
	pm	Nad
	8 am	Nad
	pm	Recovering from sedation.
	9 am	Nad
	pm	Nad
	10 am	Nad
	pm	Nad
	11 am	Nad
	pm	Nad
	12 am	Nad
	pm	Nad
	13 am	Nad
	pm	Nad
	14 am	Nad
	pm	Nad
	15 am	Nad
	pm	Nad
	16 am	Nad
	pm	Nad
	17 am	Nad
	pm	Nad
	18 am	Nad
	pm	Nad
	19 am	Nad
	pm	Loose faeces.
	20 am	Loose faeces.
	pm	Nad
	21 am	Loose faeces.
	pm	Purple urine.
	22 am	Loose faeces. Purple coloured urine.
	pm	Purple colouration of skin, tongue and gums.
	23 am	Loose faeces. Purple coloured urine.
	pm	Loose faeces. Purple coloured urine.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W15m (contd)	24 am	Loose faeces. Purple coloured urine.
	pm	Discoloured urine.
	25 am	Nad
	pm	Nad
	26 am	Nad
	pm	Nad
	27 am	Nad
	pm	Nad
	28 am	Nad
	pm	Nad
	29 am	Nad
	pm	Nad
	30 am	Nad
	pm	Purple colouration of skin, tongue and gums.
	31 am	Nad
	pm	Purple coloured urine plus tongue, gums and skin.
	32 am	Purple coloured urine.
	pm	Purple coloured urine.
	33 am	Purple coloured urine.
	pm	Purple coloured urine.
	34 am	Purple coloured urine.
	pm	Nad
	35 am	Nad
	pm	Nad
	36 am	Nad
	pm	Nad
	37 am	Nad
	pm	Nad
	38 am	Nad
	pm	Nad
	39 am	Nad
	pm	Nad
	40 am	Nad
	pm	Nad
	41 am	Nad
	pm	Nad
	42 am	Nad
	pm	Nad
	43 am	Nad
	pm	Nad
	44 am	Nad
	pm	Nad
	45 am	Nad
	pm	Nad
	46 am	Nad
	pm	Nad
	47 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W15m (contd)	48 am	Grinding teeth.
	pm	Nad
	49 am	Nad
	pm	Nad
	50 am	Nad
	pm	Nad
	51 am	Bright green/yellow urine.
	pm	Nad
	52 am	Discoloured urine.
	pm	Nad
	53 am	Nad
	pm	Nad
	54 am	Nad
	pm	Nad
	55 am	Nad
	pm	Nad
	56 am	Nad
	pm	Nad
	57 am	Nad
	pm	Nad
	58 am	Nad
	pm	Nad
	59 am	Nad
	pm	Nad
	60 am	Orange staining in tray.
	pm	Nad
	61 am	Nad
	pm	Nad
	62 am	Nad
	pm	Nad
	63 am	Nad
	pm	Recovering from anaesthesia.
	64 am	Nad
	pm	Nad
	65 am	Nad
	pm	Nad
	66 am	Nad
	pm	Nad
	67 am	Nad
	pm	Nad
	68 am	Nad
	pm	Nad
	69 am	Nad
	Pm	Nad
	70 am	Nad
	pm	Nad
	71 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W15m (contd)	72 am	Nad
	pm	Nad
	73 am	Nad
	pm	Nad
	74 am	Nad
	pm	Nad
	75 am	Nad
	pm	Nad
	76 am	Nad
	pm	Nad
	77 am	Nad
	pm	Nad
	78 am	Nad
	pm	Nad
	79 am	Nad
	pm	Nad
	80 am	Nad
	pm	Nad
	81 am	Nad
	pm	Nad
	82 am	Nad
	pm	Nad
	83 am	Nad
	pm	Nad
	84 am	Nad
	pm	Nad
	85 am	Nad
	pm	Nad
	86 am	Nad
	pm	Nad
	87 am	Nad
	pm	Nad
	88 am	Yellow staining in tray.
	pm	Yellow staining in tray.
	89 am	Nad
	pm	Nad
	90 am	Nad
	pm	Nad
	91 am	Nad
	pm	Sacrificed.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W17m	1 am	Loose faeces.
	pm	Loose faeces.
	2 am	Loose faeces.
	pm	Nad
	3 am	Loose faeces.
	pm	Loose/liquid faeces.
	4 am	Loose faeces.
	pm	Liquid faeces.
	5 am	Pale liquid faeces.
	pm	Loose/liquid faeces.
	6 am	Loose/liquid faeces.
	pm	Nad
	7 am	Loose/liquid faeces.
	pm	Loose/normal faeces.
	8 am	Loose/normal faeces.
	pm	Unsteady, recovering from sedation.
	9 am	Loose/normal faeces.
	pm	Nad
	10 am	Nad
	pm	Nad
	11 am	Nad
	pm	Nad
	12 am	Nad
	pm	Nad
	13 am	Nad
	pm	Nad
	14 am	Nad
	pm	Nad
	15 am	Nad
	pm	Nad
	16 am	Nad
	pm	Nad
	17 am	Nad
	pm	Nad
	18 am	Nad
	pm	Nad
	19 am	Nad
	pm	Nad
	20 am	Nad
	pm	Nad
	21 am	Nad
	pm	Purple coloured urine.
	22 am	Purple coloured urine.
	pm	Purple colouration of skin, tongue and gums. Discoloured urine.
	23 am	Purple coloured urine.
	pm	Purple coloured urine.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W17m (contd)	24 am	Purple coloured urine.
	pm	Quiet and huddled. Purple coloured urine.
	25 am	Quiet and huddled.
	pm	Quiet and huddled.
	26 am	Quiet. Unsteady when moving. Whole body tremors.
	pm	Quiet. Unsteady when moving. Huddled at back of cage.
	27 am	Quiet. Slightly unsteady.
	pm	Quiet. Slightly unsteady. Stereotypic activity.
	28 am	Slightly unsteady.
	pm	Quiet. Unsteady when moving. Stereotypic activity.
	29 am	Slightly unsteady.
	pm	Slightly unsteady.
	30 am	Slightly unsteady.
	pm	Alert and active. Purple colouration of skin, tongue and gums.
	31 am	Stereotypic activity.
	pm	Slightly unsteady. Purple colouration of skin, tongue and gums. Sneezing.
	32 am	Purple coloured urine.
	pm	Purple coloured urine. Slightly unsteady when moving.
	33 am	Purple coloured urine. Slightly unsteady when moving.
	pm	Huddled. Purple coloured urine.
	34 am	Nad
	pm	Nad
	35 am	Nad
	pm	Nad
	36 am	Nad
	pm	Nad
	37 am	Nad
	pm	Nad
	38 am	Nad
	pm	Nad
	39 am	Nad
	pm	Nad
	40 am	Nad
	pm	Nad
	41 am	Nad
	pm	Nad
	42 am	Nad
	pm	Nad
	43 am	Nad
	pm	Nad
	44 am	Nad
	pm	Nad
	45 am	Nad
	pm	Nad
	46 am	Nad
	pm	Nad
	47 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W17m (contd)	48 am	Nad
	pm	Nad
	49 am	Nad
	pm	Nad
	50 am	Nad
	pm	Nad
	51 am	Bright green/yellow urine.
	pm	Nad
	52 am	Discoloured urine.
	pm	Nad
	53 am	Nad
	pm	Nad
	54 am	Nad
	pm	Nad
	55 am	Nad
	pm	Nad
	56 am	Nad
	pm	Nad
	57 am	Nad
	pm	Nad
	58 am	Nad
	pm	Nad
	59 am	Nad
	pm	Nad
	60 am	Orange staining in tray.
	pm	Nad
	61 am	Nad
	pm	Nad
	62 am	Nad
	pm	Nad
	63 am	Nad
	pm	Recovering from anaesthesia.
	64 am	Nad
	pm	Nad
	65 am	Nad
	pm	Nad
	66 am	Nad
	pm	Nad
	67 am	Nad
	pm	Nad
	68 am	Nad
	pm	Nad
	69 am	Nad
	pm	Nad
	70 am	Nad
	pm	Nad
	71 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W17m (contd)	72 am	Nad
	pm	Nad
	73 am	Nad
	pm	Nad
	74 am	Nad
	pm	Nad
	75 am	Nad
	pm	Nad
	76 am	Nad
	pm	Nad
	77 am	Nad
	pm	Nad
	78 am	Nad
	pm	Nad
	79 am	Nad
	pm	Nad
	80 am	Nad
	pm	Nad
	81 am	Nad
	pm	Nad
	82 am	Nad
	pm	Nad
	83 am	Nad
	pm	Nad
	84 am	Nad
	pm	Nad
	85 am	Nad
	pm	Nad
	86 am	Nad
	pm	Nad
	87 am	Nad
	pm	Nad
	88 am	Yellow staining in tray.
	pm	Nad
	89 am	Nad
	pm	Nad
	90 am	Nad
	pm	Nad
	91 am	Nad
	pm	Sacrificed.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W16f	1 am	Loose faeces. Wound on tail slightly open. Nervous.
	pm	Nad
	2 am	Loose faeces.
	pm	Nad
	3 am	Loose faeces.
	pm	Loose/liquid faeces.
	4 am	Loose faeces.
	pm	Loose faeces.
	5 am	Loose/normal faeces. Some wound breakdown evident dorsally and on tail stump.
	pm	Nad
	6 am	Nad. Wound much improved.
	pm	Nad
	7 am	Nad
	pm	Nad
	8 am	Nad
	pm	Recovering from sedation.
	9 am	Nad
	pm	Nad
	10 am	Nad
	pm	Nad
	11 am	Nad
	pm	Nad
	12 am	Nad
	pm	Nad
	13 am	Nad
	pm	Nad
	14 am	Nad
	pm	Nad
	15 am	Nad
	pm	Nad
	16 am	Nad
	pm	Nad
	17 am	Nad
	pm	Nad
	18 am	Loose faeces.
	pm	Nad
	19 am	Loose/normal faeces.
	pm	Liquid faeces.
	20 am	Loose faeces.
	pm	No faeces.
	21am	Loose faeces.
	pm	Purple urine.
	22 am	Loose faeces. Purple urine.
	pm	Purple colouration of skin, tongue and gums. Purple urine. Purple faeces.
	23 am	Purple urine.
	pm	Purple urine. Discoloured faeces.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W16f (contd)	24 am	Purple urine.
	pm	Nad
	25 am	Nad
	pm	Nad
	26 am	Nad
	pm	Nad
	27 am	Nad
	pm	Nad
	28 am	Loose faeces.
	pm	Loose faeces.
	29 am	Loose faeces.
	pm	Loose faeces.
	30 am	Loose faeces.
	pm	Purple colouration of skin, tongue and gums.
	31 am	Loose faeces.
	pm	Purple colouration of skin, tongue and gums.
	32 am	Purple urine.
	pm	Loose faeces.
	33 am	Purple urine.
	pm	Nad
	34 am	Nad
	pm	Nad
	35 am	Nad
	pm	Nad
	36 am	Nad
	pm	Nad
	37 am	Nad
	pm	Nad
	38 am	Nad
	pm	Nad
	39 am	Nad
	pm	Nad
	40 am	Nad
	pm	Nad
	41 am	Nad
	pm	Nad
	42 am	Nad
	pm	Nad
	43 am	Nad
	pm	Nad
	44 am	Nad
	pm	Nad
	45 am	Nad
	pm	Nad
	46 am	Nad
	pm	Nad
	47 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W16f (contd)	48 am	Nad
	pm	Nad
	49 am	Loose/liquid Faeces.
	pm	Loose/normal faeces.
	50 am	Nad
	pm	Nad
	51 am	Bright green/yellow urine.
	pm	Nad
	52 am	Discoloured urine.
	pm	Nad
	53 am	Nad
	pm	Nad
	54 am	Nad
	pm	Nad
	55 am	Nad
	pm	Nad
	56 am	Nad
	pm	Nad
	57 am	Nad
	pm	Nad
	58 am	Nad
	pm	Nad
	59 am	Nad
	pm	Nad
	60 am	Orange staining in tray.
	pm	Nad
	61 am	Nad
	pm	Nad
	62 am	Nad
	pm	Nad
	63 am	Nad
	pm	Recovering from anaesthesia.
	64 am	Nad
	pm	Nad
	65 am	Nad
	pm	Nad
	66 am	Nad
	pm	Nad
	67 am	Nad
	pm	Nad
	68 am	Nad
	pm	Nad
	69 am	Nad
	pm	Nad
	70 am	Nad
	pm	Nad
	71 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W16f (contd)	72 am	Nad
	pm	Nad
	73 am	Nad
	pm	Nad
	74 am	Nad
	pm	Nad
	75 am	Nad
	pm	Nad
	76 am	Nad
	pm	Nad
	77 am	Nad
	pm	Nad
	78 am	Nad
	pm	Nad
	79 am	Nad
	pm	Nad
	80 am	Nad
	pm	Nad
	81 am	Nad
	pm	Nad
	82 am	Nad
	pm	Nad
	83 am	Nad
	pm	Nad
	84 am	Nad
	pm	Nad
	85 am	Nad
	pm	Nad
	86 am	Nad
	pm	Nad
	87 am	Nad
	pm	Nad
	88 am	Yellow staining in tray
	pm	Nad
	89 am	Nad
	pm	Nad
	90 am	Nad
	pm	Nad
	91 am	Nad
	pm	Sacrificed.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W22f	1 am	Loose faeces.
	pm	Nad
	2 am	Loose faeces.
	pm	Nad
	3 am	Loose faeces.
	pm	Loose/normal faeces.
	4 am	Loose faeces.
	pm	Pale liquid faeces. Small lump in mid ventral area of tail.
	5 am	Liquid faeces. Some wound breakdown evident dorsally and on tail stump.
	pm	Liquid faeces. Small swelling in ventral area of tail.
	6 am	Liquid faeces. Wound much improved.
	pm	Nad
	7 am	Loose faeces.
	pm	Nad
	8 am	Nad
	pm	Recovering from sedation
	9 am	Nad
	pm	Nad
	10 am	Nad
	pm	Nad
	11 am	Nad
	pm	Nad
	12 am	Nad
	pm	Nad
	13 am	Nad
	pm	Nad
	14 am	Nad
	pm	Nad
	15 am	Nad
	pm	Nad
	16 am	Nad
	pm	Nad
	17 am	Nad
	pm	Nad
	18 am	Nad
	pm	Nad
	19 am	Nad
	pm	Nad
	20 am	Nad
	pm	Nad
	21 am	Nad
	pm	Purple urine.
	22 am	Vomit in tray. Purple urine.
	pm	Purple colouration of skin, tongue and gums.
	23 am	Purple urine.
	pm	Purple urine.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W22f (contd)	24 am	Purple urine.
	pm	Purple urine.
	25 am	Nad
	pm	Nad
	26 am	Nad
	pm	Nad
	27 am	Nad
	pm	Nad
	28 am	Nad
	pm	Nad
	29 am	Nad
	pm	Nad
	30 am	Nad
	pm	Purple colouration of skin, tongue and gums..
	31 am	Nad
	pm	Purple colouration of skin, tongue and gums. Purple faeces.
	32 am	Purple urine.
	pm	Purple urine.
	33 am	Purple urine.
	pm	Nad
	34 am	Nad
	pm	Nad
	35 am	Nad
	pm	Recovering from anaesthesia.
	36 am	Nad
	pm	Nad
	37 am	Nad
	pm	Nad
	38 am	Nad
	pm	Nad
	39 am	Nad
	pm	Nad
	40 am	Nad
	pm	Nad
	41 am	Nad
	pm	Nad
	42 am	Nad
	pm	Nad
	43 am	Nad
	pm	Nad
	44 am	Nad
	pm	Nad
	45 am	Nad
	pm	Nad
	46 am	Nad
	pm	Nad
	47 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W22f (contd)	48 am	Nad
	pm	Nad
	49 am	Nad
	pm	Nad
	50 am	Nad
	pm	Nad
	51 am	Bright green/yellow urine.
	pm	Nad
	52 am	Discoloured urine.
	pm	Nad
	53 am	Nad
	pm	Nad
	54 am	Nad
	pm	Nad
	55 am	Nad
	pm	Nad
	56 am	Nad
	pm	Quiet.
	57 am	Nad
	pm	Nad
	58 am	Nad
	pm	Nad
	59 am	Nad
	pm	Nad
	60 am	Orange staining in tray.
	pm	Nad
	61 am	Nad
	pm	Nad
	62 am	Nad
	pm	Nad
	63 am	Nad
	pm	Recovering from anaesthesia.
	64 am	Nad
	pm	Nad
	65 am	Nad
	pm	Nad
	66 am	Nad
	pm	Nad
	67 am	Nad
	pm	Nad
	68 am	Nad
	pm	Nad
	69 am	Nad
	pm	Nad
	70 am	Nad
	pm	Nad
	71 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W22f (contd)	72 am	Nad
	pm	Nad
	73 am	Nad
	pm	Nad
	74 am	Nad
	pm	Nad
	75 am	Nad
	pm	Nad
	76 am	Nad
	pm	Nad
	77 am	Nad
	pm	Nad
	78 am	Nad
	pm	Nad
	79 am	Nad
	pm	Nad
	80 am	Nad
	pm	Nad
	81 am	Nad
	pm	Nad
	82 am	Nad
	pm	Nad
	83 am	Nad
	pm	Nad
	84 am	Nad
	pm	Nad
	85 am	Nad
	pm	Nad
	86 am	Nad
	pm	Nad
	87 am	Nad
	pm	Nad
	88 am	Yellow staining in tray.
	pm	Nad
	89 am	Nad
	pm	Nad
	90 am	Nad
	pm	Nad
	91 am	Nad
	pm	Sacrificed.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W25m	1 am	Nad
	pm	Nad
	2 am	Nad
	pm	Nad
	3 am	Nad
	pm	Nad
	4 am	Nad
	pm	Nad
	5 am	Nad
	pm	Nad
	6 am	Nad
	pm	Nad
	7 am	Nad
	pm	Nad
	8 am	Nad
	pm	Nad
	9 am	Nad
	pm	Nad
	10 am	Nad
	pm	Nad
	11 am	Nad
	pm	Nad
	12 am	Nad
	pm	Nad
	13 am	Nad
	pm	Nad
	14 am	Nad
	pm	Nad
	15 am	Nad
	pm	Nad
	16 am	Nad
	pm	Nad
	17 am	Nad
	pm	Nad
	18 am	Nad
	pm	Nad
	19 am	Nad
	pm	Nad
	20 am	Nad
	pm	Purple coloured skin, tongue and gums.
	21 am	Purple urine.
	pm	Purple coloured skin, tongue and gums.
	22 am	Purple urine.
	pm	Purple staining in tray.
	23 am	Nad
	pm	Dark red/purple faeces.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W25m (contd)	24 am	Nad
	pm	Nad
	25 am	Nad
	pm	Nad
	26 am	Nad
	pm	Nad
	27 am	Nad
	pm	Nad
	28 am	Nad
	pm	Nad
	29 am	Nad
	pm	Purple urine. Purple coloured skin, tongue and gums.
	30 am	Purple urine.
	pm	Purple staining in tray.
	31 am	Purple urine.
	pm	Purple urine.
	32 am	Purple urine.
	pm	Purple urine.
	33 am	Purple urine.
	pm	Nad
	34 am	Nad
	pm	Nad
	35 am	Nad
	pm	Nad
	36 am	Nad
	pm	Nad
	37 am	Nad
	pm	Nad
	38 am	Nad
	pm	Nad
	39 am	Nad
	pm	Nad
	40 am	Nad
	pm	Nad
	41 am	Nad
	pm	Nad
	42 am	Nad
	pm	Nad
	43 am	Nad
	pm	Nad
	44 am	Nad
	pm	Nad
	45 am	Nad
	pm	Nad
	46 am	Nad
	pm	Nad
	47 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W25m (contd)	48 am	Nad
	pm	Nad
	49 am	Orange staining
	pm	Nad
	50 am	Orange staining in tray
	pm	Nad
	51 am	Nad
	pm	Nad
	52 am	Nad
	pm	Nad
	53 am	Nad
	pm	Nad
	54 am	Nad
	pm	Nad
	55 am	Nad
	pm	Orange coloured urine.
	56 am	Nad
	pm	Nad
	57 am	Nad
	pm	Nad
	58 am	Orange staining in tray.
	pm	Nad
	59 am	Orange staining in tray.
	pm	Nad
	60 am	Nad
	pm	Nad
	61 am	Nad
	pm	Nad
	62 am	Nad
	pm	Nad
	63 am	Nad
	pm	Recovering from sedation.
	64 am	Nad
	pm	Nad
	65 am	Nad
	pm	Nad
	66 am	Nad
	pm	Nad
	67 am	Nad
	pm	Nad
	68 am	Nad
	pm	Nad
	69 am	Nad
	pm	Nad
	70 am	Nad
	pm	Nad
	71 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W25m (contd)	72 am	Nad
	pm	Nad
	73 am	Nad
	pm	Nad
	74 am	Nad
	pm	Nad
	75 am	Nad
	pm	Nad
	76 am	Nad
	pm	Nad
	77 am	Nad
	pm	Nad
	78 am	Yellow staining in tray.
	pm	Nad
	79 am	Nad
	pm	Nad
	80 am	Nad
	pm	Nad
	81 am	Nad
	pm	Nad
	82 am	Nad
	pm	Nad
	83 am	Nad
	pm	Nad
	84 am	Nad
	pm	Nad
	85 am	Nad
	pm	Nad
	86 am	Nad
	pm	Nad
	87 am	Nad
	pm	Nad
	88 am	Nad
	pm	Nad
	89 am	Nad
	pm	Nad
	90 am	Sacrificed.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W31m	1 am	Nad
	pm	Nad
	2 am	Nad
	pm	Nad
	3 am	Nad
	pm	Nad
	4 am	Nad
	pm	Nad
	5 am	Nad
	pm	Nad
	6 am	Nad
	pm	Nad
	7 am	Nad
	pm	Nad
	8 am	Nad
	pm	Nad
	9 am	Nad
	pm	Nad
	10 am	Nad
	pm	Nad
	11 am	Nad
	pm	Nad
	12 am	Nad
	pm	Nad
	13 am	Nad
	pm	Nad
	14 am	Nad
	pm	Nad
	15 am	Nad
	pm	Nad
	16 am	Nad
	pm	Nad
	17 am	Nad
	pm	Nad
	18 am	Nad
	pm	Nad
	19 am	Nad
	pm	Nad
	20 am	Nad
	pm	Purple coloured skin, tongue and gums.
	21 am	Purple urine.
	pm	Purple coloured skin, tongue and gums.
	22 am	Purple urine.
	pm	Purple staining in tray.
	23 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W31m (contd)	24 am	Nad
	pm	Nad
	25 am	Nad
	pm	Nad
	26 am	Nad
	pm	Nad
	27 am	Nad
	pm	Nad
	28 am	Nad
	pm	Nad
	29 am	Nad
	pm	Purple urine. Purple coloured skin.
	30 am	Purple urine.
	pm	Purple stain in tray
	31 am	Purple urine.
	pm	Purple urine.
	32 am	Purple urine.
	pm	Nad
	33 am	Nad
	pm	Nad
	34 am	Nad
	pm	Nad
	35 am	Nad
	pm	Nad
	36 am	Nad
	pm	Nad
	37 am	Nad
	pm	Nad
	38 am	Nad
	pm	Nad
	39 am	Nad
	pm	Nad
	40 am	Nad
	pm	Nad
	41 am	Nad
	pm	Nad
	42 am	Nad
	pm	Nad
	43 am	Nad
	pm	Nad
	44 am	Nad
	pm	Nad
	45 am	Nad
	pm	Nad
	46 am	Nad
	pm	Nad
	47 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W31m (contd)	48 am	Nad
	pm	Nad
	49 am	Orange staining in tray.
	pm	Nad
	50 am	Orange staining in tray.
	pm	Nad
	51 am	Nad
	pm	Nad
	52 am	Nad
	pm	Nad
	53 am	Nad
	pm	Nad
	54 am	Nad
	pm	Nad
	55 am	Nad
	pm	Orange coloured urine.
	56 am	Nad
	pm	Nad
	57 am	Nad
	pm	Nad
	58 am	Orange staining in tray.
	pm	Nad
	59 am	Orange staining in tray.
	pm	Nad
	60 am	Nad
	pm	Nad
	61 am	Nad
	pm	Nad
	62 am	Nad
	pm	Nad
	63 am	Nad
	pm	Recovering from sedation.
	64 am	Nad
	pm	Nad
	65 am	Nad
	pm	Nad
	66 am	Nad
	pm	Nad
	67 am	Nad
	pm	Nad
	68 am	Nad
	pm	Nad
	69 am	Nad
	pm	Nad
	70 am	Nad
	pm	Nad
	71 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W31m (contd)	73 am	Nad
	pm	Nad
	74 am	Nad
	pm	Nad
	75 am	Nad
	pm	Nad
	76 am	Nad
	pm	Nad
	77 am	Nad
	pm	Nad
	78 am	Yellow staining in tray.
	pm	Nad
	79 am	Nad
	pm	Nad
	80 am	Nad
	pm	Nad
	81 am	Nad
	pm	Nad
	82 am	Nad
	pm	Nad
	83 am	Nad
	pm	Nad
	84 am	Nad
	pm	Nad
	85 am	Nad
	pm	Nad
	86 am	Nad
	pm	Nad
	87 am	Nad
	pm	Nad
	88 am	Nad
	pm	Nad
	89 am	Nad
	pm	Nad
	90 am	Nad
	pm	Nad
	91 am	Sacrificed

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W30f	1 am	Nad
	pm	Nad
	2 am	Nad
	pm	Nad
	3 am	Nad
	pm	Nad
	4 am	Nad
	pm	Nad
	5 am	Nad
	pm	Quiet. Recovering from sedation.
	6 am	Nad
	pm	Nad
	7 am	Nad
	pm	Nad
	8 am	Nad
	pm	Nad
	9 am	Nad
	pm	Nad
	10 am	Nad
	pm	Nad
	11 am	Nad
	pm	Nad
	12 am	Nad
	pm	Nad
	13 am	Nad
	pm	Nad
	14 am	Piloerection.
	pm	Piloerection.
	15 am	Piloerection.
	pm	Piloerection.
	16 am	Piloerection.
	pm	Piloerection.
	17 am	Piloerection.
	pm	Piloerection.
	18 am	Piloerection.
	pm	Piloerection.
	19 am	Piloerection.
	pm	Piloerection.
	20 am	Piloerection.
	pm	Purple colouration of skin, tongue and gums.
	21 am	Purple urine.
	pm	Purple urine. Purple colouration of skin, tongue and gums.
	22 am	Purple urine.
	pm	Purple staining in tray.
	23 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W30f (contd)	24 am	Blood spots on tray.
	pm	Nad
	25 am	Nad
	pm	Nad
	26 am	Nad
	pm	Nad
	27 am	Nad
	pm	Nad
	28 am	Nad
	pm	Nad
	29 am	Loose faeces.
	pm	Loose faeces. Purple colouration of skin, tongue and gums. Purple urine.
	30 am	Purple urine in tray.
	pm	Purple stain in tray.
	31 am	Purple urine. Loose faeces.
	pm	Purple urine. Loose faeces.
	32 am	Purple urine.
	pm	Nad
	33 am	Nad
	pm	Nad
	34 am	Nad
	pm	Nad
	35 am	Nad
	pm	Nad
	36 am	Nad
	pm	Nad
	37 am	Nad
	pm	Nad
	38 am	Nad
	pm	Nad
	39 am	Nad
	pm	Nad
	40 am	Nad
	pm	Nad
	41 am	Nad
	pm	Nad
	42 am	Nad
	pm	Nad
	43 am	Nad
	pm	Nad
	44 am	Nad
	pm	Nad
	45 am	Nad
	pm	Nad
	46 am	Nad
	pm	Nad
	47 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W30f (contd)	48 am	Nad
	pm	Nad
	49 am	Orange staining
	pm	Nad
	50 am	Orange staining in tray.
	pm	Nad
	51 am	Nad
	pm	Nad
	52 am	Nad
	pm	Nad
	53 am	Nad
	pm	Nad
	54 am	Nad
	pm	Nad
	55 am	Nad
	pm	Nad
	56 am	Nad
	pm	Nad
	57 am	Nad
	pm	Nad
	58 am	Orange staining in tray.
	pm	Nad
	59 am	Orange staining in tray.
	pm	Nad
	60 am	Nad
	pm	Nad
	61 am	Nad
	pm	Nad
	62 am	Nad
	pm	Nad
	63 am	Nad
	pm	Nad
	64 am	Nad
	pm	Nad
	65 am	Nad
	pm	Nad
	66 am	Nad
	pm	Quiet and huddled.
	67 am	Nad
	pm	Nad
	68 am	Nad
	pm	Nad
	69 am	Nad
	pm	Nad
	70 am	Nad
	pm	Nad
	71 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W30f (contd)	72 am	Nad
	pm	Nad
	73 am	Nad
	pm	Nad
	74 am	Nad
	pm	Nad
	75 am	Nad
	pm	Nad
	76 am	Nad
	pm	Nad
	77 am	Nad
	pm	Nad
	78 am	Yellow staining in tray.
	pm	Nad
	79 am	Nad
	pm	Nad
	80 am	Nad
	pm	Nad
	81 am	Nad
	pm	Nad
	82 am	Nad
	pm	Nad
	83 am	Nad
	pm	Nad
	84 am	Nad
	pm	Nad
	85 am	Nad
	pm	Nad
	86 am	Nad
	pm	Nad
	87 am	Nad
	pm	Nad
	88 am	Nad
	pm	Nad
	89 am	Nad
	pm	Nad
	90 am	Nad`
	pm	Sacrificed.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W36f	1 am	Small amount of blood in tray
	pm	Nad
	2 am	Nad
	pm	Nad
	3 am	Nad
	pm	Nad
	4 am	Nad
	pm	Nad
	5 am	Nad
	pm	Quiet.
	6 am	Quiet.
	pm	Nad
	7 am	Nad
	pm	Nad
	8 am	Nad
	pm	Nad
	9 am	Nad
	pm	Nad
	10 am	Nad
	pm	Nad
	11 am	Nad
	pm	Nad
	12 am	Nad
	pm	Nad
	13 am	Loose/normal faeces.
	pm	Loose/normal faeces.
	14 am	Nad
	pm	Nad
	15 am	Nad
	pm	Nad
	16 am	Nad
	pm	Nad
	17 am	Nad
	pm	Nad
	18 am	Nad
	pm	Nad
	19 am	Nad
	pm	Nad
	20 am	Nad
	pm	Purple colouration of skin, tongue and gums.
	21 am	Purple urine.
	pm	Purple colouration of skin, tongue and gums.
	22 am	Purple urine.
	pm	Purple staining in tray. Discoloured faeces.
	23 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W36f (contd)	24 am	Nad
	pm	Nad
	25 am	Nad
	pm	Nad
	26 am	Nad
	pm	Nad
	27 am	Nad
	pm	Nad
	28 am	Nad
	pm	Nad
	29 am	Nad
	pm	Purple urine. Purple colouration of skin, tongue and gums.
	30 am	Purple urine.
	pm	Purple stain in tray.
	31 am	Purple urine.
	pm	Purple urine.
	32 am	Purple urine.
	pm	Nad
	33 am	Nad
	pm	Nad
	34 am	Nad
	pm	Nad
	35 am	Nad
	pm	Nad
	36 am	Nad
	pm	Nad
	37 am	Nad
	pm	Nad
	38 am	Nad
	pm	Nad
	39 am	Nad
	pm	Nad
	40 am	Nad
	pm	Nad
	41 am	Nad
	pm	Nad
	42 am	Nad
	pm	Nad
	43 am	Nad
	pm	Nad
	44 am	Nad
	pm	Nad
	45 am	Nad
	pm	Nad
	46 am	Nad
	pm	Nad
	47 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W36f (contd)	48 am	Nad
	pm	Nad
	49 am	Orange staining in tray.
	pm	Nad
	50 am	Orange staining in tray.
	pm	Nad
	51 am	Nad
	pm	Nad
	52 am	Nad
	pm	Nad
	53 am	Nad
	pm	Nad
	54 am	Nad
	pm	Nad
	55 am	Nad
	pm	Orange coloured urine.
	56 am	Nad
	pm	Nad
	57 am	Nad
	pm	Nad
	58 am	Orange staining in tray.
	pm	Nad
	59 am	Orange staining in tray.
	pm	Nad
	60 am	Nad
	pm	Nad
	61 am	Nad
	pm	Nad
	62 am	Nad
	pm	Nad
	63 am	Nad
	pm	Recovering from sedation.
	64 am	Nad
	pm	Nad
	65 am	Nad
	pm	Nad
	66 am	Nad
	pm	Quiet and huddled.
	67 am	Nad
	pm	Nad
	68 am	Nad
	pm	Nad
	69 am	Nad
	pm	Nad
	70 am	Nad
	pm	Nad
	71 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W36f (contd)	72 am	Nad
	pm	Nad
	73 am	Nad
	pm	Nad
	74 am	Nad
	pm	Nad
	75 am	Nad
	pm	Nad
	76 am	Nad
	pm	Nad
	77 am	Nad
	pm	Nad
	78 am	Yellow staining in tray.
	pm	Nad
	79 am	Nad
	pm	Nad
	80 am	Nad
	pm	Nad
	81 am	Nad
	pm	Nad
	82 am	Nad
	pm	Nad
	83 am	Nad
	pm	Nad
	84 am	Nad
	pm	Nad
	85 am	Nad
	pm	Nad
	86 am	Nad
	pm	Nad
	87 am	Nad
	pm	Nad
	88 am	Nad
	pm	Nad
	89 am	Nad
	pm	Nad
	90 am	Nad
	pm	Sacrificed.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W45m	1 am	Nad
	pm	Nad
	2 am	Nad
	pm	Nad
	3 am	Nad
	pm	Nad
	4 am	Nad
	pm	Nad
	5 am	Nad
	pm	Nad
	6 am	Nad
	pm	Nad
	7 am	Nad
	pm	Nad
	8 am	Nad
	pm	Nad
	9 am	Nad
	pm	Nad
	10 am	Nad
	pm	Nad
	11 am	Nad
	pm	Nad
	12 am	Nad
	pm	Nad
	13 am	Nad
	pm	Nad
	14 am	Nad
	pm	Nad
	15 am	Nad
	pm	Nad
	16 am	Nad
	pm	Nad
	17 am	Nad
	pm	Nad
	18 am	Nad
	pm	Nad
	19 am	Nad
	pm	Nad
	20 am	Nad
	pm	Nad
	21 am	Nad
	pm	Purple colouration of face, gums and limbs
	22 am	Nad
	pm	Purple colouration all over body.
	23 am	Purple staining in tray.
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W45m (contd)	24 am	Nad
	pm	Nad
	25 am	Nad
	pm	Nad
	26 am	Nad
	pm	Nad
	27 am	Nad
	pm	Nad
	28 am	Nad
	pm	Nad
	29 am	Nad
	pm	Nad
	30 am	Nad
	pm	Purple colouration all over body.
	31 am	Purple staining in tray.
	pm	Purple colouration all over body.
	32 am	Purple staining in tray.
	pm	Nad
	33 am	Nad
	pm	Nad
	34 am	Nad
	pm	Nad
	35 am	Nad
	pm	Nad
	36 am	Nad
	pm	Recovering from sedation.
	37 am	Nad
	pm	Nad
	38 am	Nad
	pm	Nad
	39 am	Nad
	pm	Nad
	40 am	Nad
	pm	Nad
	41 am	Nad
	pm	Nad
	42 am	Nad
	pm	Nad
	43 am	Nad
	pm	Nad
	44 am	Nad
	pm	Nad
	45 am	Nad
	pm	Nad
	46 am	Nad
	pm	Nad
	47 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W45m (contd)	48 am	Nad
	pm	Nad
	49 am	Nad
	pm	Nad
	50 am	Yellow staining.
	pm	Nad
	51 am	Yellow staining in tray.
	pm	Nad
	52 am	Nad
	pm	Nad
	53 am	Nad
	pm	Nad
	54 am	Nad
	pm	Nad
	55 am	Nad
	pm	Nad
	56 am	Nad
	pm	Nad
	57 am	Nad
	pm	Nad
	58 am	Nad
	pm	Yellow staining in tray.
	59 am	Yellow staining in tray.
	pm	Recovering from sedation.
	60 am	Nad
	pm	Nad
	61 am	Nad
	pm	Nad
	62 am	Nad
	pm	Nad
	63 am	Nad
	pm	Nad
	64 am	Nad
	pm	Nad
	65 am	Nad
	pm	Nad
	66 am	Nad
	pm	Nad
	67 am	Nad
	pm	Nad
	68 am	Nad
	pm	Nad
	69 am	Nad
	pm	Nad
	70 am	Nad
	pm	Nad
	71 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W45m (contd)	72 am	Nad
	pm	Nad
	73 am	Nad
	pm	Nad
	74 am	Nad
	pm	Nad
	75 am	Nad
	pm	Nad
	76 am	Nad
	pm	Nad
	77 am	Nad
	pm	Nad
	78 am	Nad
	pm	Nad
	79 am	Nad
	pm	Nad
	80 am	Nad
	pm	Nad
	81 am	Nad
	pm	Nad
	82 am	Nad
	pm	Nad
	83 am	Nad
	pm	Nad
	84 am	Nad
	pm	Nad
	85 am	Nad
	pm	Nad
	86 am	Nad
	pm	Nad
	87 am	Nad
	pm	Nad
	88 am	Nad
	pm	Nad
	89 am	Nad
	pm	Nad
	90 am	Nad
	pm	Nad
	91 am	Nad
	pm	Nad
	92 am	Nad
	pm	Nad
	93 am	Nad
	pm	Nad
	94 am	Nad
	pm	Nad
	95 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W45m (contd)	96 am pm 97 am	Nad Nad Sacrificed.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W139m	1 am	Nad
	pm	Quiet.
	2 am	Nad
	pm	Nad
	3 am	Nad
	pm	Nad
	4 am	Nad
	pm	Nad
	5 am	Nad
	pm	Nad
	6 am	Nad
	pm	Nad
	7 am	Nad
	pm	Nad
	8 am	Nad
	pm	Quiet.
	9 am	Nad
	pm	Nad
	10 am	Nad
	pm	Nad
	11 am	Nad
	pm	Nad
	12 am	Nad
	pm	Nad
	13 am	Nad
	pm	Nad
	14 am	Nad
	pm	Nad
	15 am	Nad
	pm	Nad
	16 am	Nad
	pm	Nad
	17 am	Nad
	pm	Nad
	18 am	Nad
	pm	Nad
	19 am	Nad
	pm	Nad
	20 am	Nad
	pm	Nad
	21 am	Nad
	pm	Purple colouration of gums, face and limbs.
	22 am	Purple staining.
	pm	Purple colouration all over body.
	23 am	Purple staining in tray.
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W139m (contd)	24 am	Nad
	pm	Nad
	25 am	Nad
	pm	Nad
	26 am	Nad
	pm	Nad
	27 am	Nad
	pm	Nad
	28 am	Nad
	pm	Nad
	29 am	Nad
	pm	Nad
	30 am	Nad
	pm	Purple colouration all over body.
	31 am	Purple staining in tray.
	pm	Purple colouration all over body.
	32 am	Purple staining in tray.
	pm	Nad
	33 am	Nad
	pm	Nad
	34 am	Nad
	pm	Nad
	35 am	Nad
	pm	Recovering from sedation.
	36 am	Nad
	pm	Nad
	37 am	Nad
	pm	Nad
	38 am	Nad
	pm	Nad
	39 am	Nad
	pm	Nad
	40 am	Nad
	pm	Nad
	41 am	Nad
	pm	Nad
	42 am	Nad
	pm	Nad
	43 am	Nad
	pm	Nad
	44 am	Nad
	pm	Nad
	45 am	Nad
	pm	Nad
	46 am	Nad
	pm	Nad
	47 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W139m (contd)	48 am	Nad
	pm	Nad
	49 am	Nad
	pm	Nad
	50 am	Yellow staining in tray.
	pm	Nad
	51 am	Yellow staining in tray.
	pm	Nad
	52 am	Nad
	pm	Nad
	53 am	Nad
	pm	Nad
	54 am	Nad
	pm	Nad
	55 am	Nad
	pm	Nad
	56 am	Nad
	pm	Nad
	57 am	Nad
	pm	Nad
	58 am	Nad
	pm	Yellow staining in tray.
	59 am	Yellow staining in tray.
	pm	Recovering from sedation.
	60 am	Nad
	pm	Nad
	61 am	Nad
	pm	Nad
	62 am	Nad
	pm	Nad
	63 am	Nad
	pm	Nad
	64 am	Nad
	pm	Nad
	65 am	Nad
	pm	Nad
	66 am	Nad
	pm	Nad
	67 am	Nad
	pm	Nad
	68 am	Nad
	pm	Nad
	69 am	Nad
	pm	Nad
	70 am	Nad
	pm	Nad
	71 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W139m (contd)	72 am	Nad
	pm	Nad
	73 am	Nad
	pm	Nad
	74 am	Nad
	pm	Nad
	75 am	Nad
	pm	Nad
	76 am	Nad
	pm	Nad
	77 am	Nad
	pm	Nad
	78 am	Nad
	pm	Nad
	79 am	Nad
	pm	Nad
	80 am	Nad
	pm	Nad
	81 am	Nad
	pm	Nad
	82 am	Nad
	pm	Nad
	83 am	Nad
	pm	Nad
	84 am	Nad
	pm	Nad
	85 am	Nad
	pm	Nad
	86 am	Nad
	pm	Nad
	87 am	Nad
	pm	Nad
	88 am	Nad
	pm	Nad
	89 am	Nad
	pm	Nad
	90 am	Nad
	pm	Nad
	91 am	Nad
	pm	Nad
	92 am	Nad
	pm	Nad
	93 am	Nad
	pm	Nad
	94 am	Nad
	pm	Nad
	95 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W139m (contd)	96 am pm 97 am	Nad Nad Sacrificed.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W42f	1 am	Blood in tray, from tail.
	pm	Nad
	2 am	Nad
	pm	Nad
	3 am	Nad
	pm	Nad
	4 am	Nad
	pm	Nad
	5 am	Nad
	pm	Nad
	6 am	Nad
	pm	Nad
	7 am	Nad
	pm	Nad
	8 am	Nad
	pm	Nad
	9 am	Nad
	pm	Nad
	10 am	Nad
	pm	Nad
	11 am	Nad
	pm	Nad
	12 am	Nad
	pm	Nad
	13 am	Nad
	pm	Nad
	14 am	Nad
	pm	Nad
	15 am	Nad
	pm	Nad
	16 am	Nad
	pm	Nad
	17 am	Nad
	pm	Nad
	18am	Nad
	pm	Nad
	19 am	Nad
	pm	Nad
	20 am	Nad
	pm	Nad
	21 am	Nad
	pm	Purple colouration of gums, face and limbs.
	22 am	Purple staining.
	pm	Purple colouration all over body.
	23 am	Purple staining in tray.
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W42f (contd)	24 am	Nad
	pm	Nad
	25 am	Nad
	pm	Nad
	26 am	Nad
	pm	Nad
	27 am	Nad
	pm	Nad
	28 am	Nad
	pm	Nad
	29 am	Nad
	pm	Nad
	30 am	Nad
	pm	Purple colouration all over body.
	31 am	Purple staining on tray
	pm	Purple colouration all over body.
	32 am	Purple staining on tray
	pm	Nad
	33 am	Nad
	pm	Nad
	34 am	Nad
	pm	Nad
	35 am	Nad
	pm	Nad
	36 am	Nad
	pm	Recovering from sedation.
	37 am	Nad
	pm	Nad
	38 am	Nad
	pm	Nad
	39 am	Nad
	pm	Nad
	40 am	Nad
	pm	Nad
	41 am	Nad
	pm	Nad
	42 am	Nad
	pm	Nad
	43 am	Nad
	pm	Nad
	44 am	Nad
	pm	Nad
	45 am	Nad
	pm	Nad
	46 am	Nad
	pm	Nad
	47 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W42f (contd)	48 am	Nad
	pm	Nad
	49 am	Nad
	pm	Nad
	50 am	Yellow staining.
	pm	Nad
	51 am	Yellow staining in tray.
	pm	Nad
	52 am	Nad
	pm	Nad
	53 am	Nad
	pm	Nad
	54 am	Nad
	pm	Nad
	55 am	Nad
	pm	Nad
	56 am	Nad
	pm	Nad
	57 am	Nad
	pm	Nad
	58 am	Nad
	pm	Yellow staining in tray.
	59 am	Yellow staining in tray.
	pm	Recovering from sedation.
	60 am	Nad
	pm	Nad
	61 am	Nad
	pm	Nad
	62 am	Nad
	pm	Nad
	63 am	Nad
	pm	Nad
	64 am	Nad
	pm	Nad
	65 am	Nad
	pm	Nad
	66 am	Nad
	pm	Nad
	67 am	Nad
	pm	Nad
	68 am	Nad
	pm	Nad
	69 am	Nad
	pm	Nad
	70 am	Nad
	pm	Nad
	71 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W42f (contd)	72 am	Nad
	pm	Nad
	73 am	Nad
	pm	Nad
	74 am	Nad
	pm	Nad
	75 am	Nad
	pm	Nad
	76 am	Nad
	pm	Nad
	77 am	Nad
	pm	Nad
	78 am	Loose faeces.
	pm	Nad
	79 am	Nad
	pm	Nad
	80 am	Loose faeces.
	pm	Nad
	81 am	Nad
	pm	Nad
	82 am	Nad
	pm	Nad
	83 am	Nad
	pm	Nad
	84 am	Nad
	pm	Nad
	85 am	Nad
	pm	Nad
	86 am	Nad
	pm	Nad
	87 am	Nad
	pm	Nad
	88 am	Nad
	pm	Nad
	89 am	Nad
	pm	Nad
	90 am	Nad
	pm	Nad
	91 am	Nad
	pm	Nad
	92 am	Nad
	pm	Nad
	93 am	Nad
	pm	Nad
	94 am	Nad
	pm	Nad
	95 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W42f (contd)	96 am	Nad
	pm	Nad
	97 am	Nad
	pm	Sacrificed.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W280f	1 am	Nad
	pm	Nad
	2 am	Nad
	pm	Nad
	3 am	Nad
	pm	Nad
	4 am	Nad
	pm	Nad
	5 am	Nad
	pm	Nad
	6 am	Nad
	pm	Nad
	7 am	Nad
	pm	Nad
	8 am	Nad
	pm	Nad
	9 am	Nad
	pm	Nad
	10 am	Nad
	pm	Nad
	11 am	Nad
	pm	Nad
	12 am	Nad
	pm	Nad
	13 am	Nad
	pm	Nad
	14 am	Nad
	pm	Nad
	15 am	Nad
	pm	Nad
	16 am	Nad
	pm	Nad
	17 am	Nad
	pm	Nad
	18 am	Nad
	pm	Nad
	19 am	Nad
	pm	Nad
	20 am	Nad
	pm	Nad
	21 am	Nad
	pm	Purple colouration of gums, face and limbs.
	22 am	Purple staining.
	pm	Purple colouration all over body.
	23 am	Purple staining in tray.
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W280f	24 am	Nad
	pm	Nad
	25 am	Nad
	pm	Nad
	26 am	Nad
	pm	Nad
	27 am	Nad
	pm	Nad
	28 am	Nad
	pm	Nad
	29 am	Nad
	pm	Nad
	30 am	Nad
	pm	Purple colouration all over body.
	31 am	Purple staining in tray.
	pm	Purple colouration all over body.
	32 am	Purple staining in tray.
	pm	Nad
	33 am	Nad
	pm	Nad
	34 am	Nad
	pm	Nad
	35 am	Nad
	pm	Nad
	36 am	Nad
	pm	Recovery from sedation.
	37 am	Nad
	pm	Nad
	38 am	Nad
	pm	Nad
	39 am	Nad
	pm	Nad
	40 am	Nad
	pm	Nad
	41 am	Nad
	pm	Nad
	42 am	Nad
	pm	Nad
	43 am	Nad
	pm	Nad
	44 am	Nad
	pm	Nad
	45 am	Nad
	pm	Nad
	46 am	Nad
	pm	Nad
	47 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W280f (contd)	48 am	Nad
	pm	Nad
	49 am	Nad
	pm	Nad
	50 am	Yellow staining in tray.
	pm	Nad
	51 am	Yellow staining in tray.
	pm	Nad
	52 am	Nad
	pm	Nad
	53 am	Nad
	pm	Nad
	54 am	Nad
	pm	Nad
	55 am	Nad
	pm	Nad
	56 am	Nad
	pm	Nad
	57 am	Nad
	pm	Nad
	58 am	Nad
	pm	Yellow staining in tray.
	59 am	Yellow staining in tray.
	pm	Recovering from sedation.
	60 am	Nad
	pm	Nad
	61 am	Nad
	pm	Nad
	62 am	Nad
	pm	Nad
	63 am	Nad
	pm	Nad
	64 am	Nad
	pm	Nad
	65 am	Nad
	pm	Nad
	66 am	Nad
	pm	Nad
	67 am	Nad
	pm	Nad
	68 am	Nad
	pm	Nad
	69 am	Nad
	pm	Nad
	70 am	Nad
	pm	Nad
	71 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W280f (contd)	72 am	Nad
	pm	Nad
	73 am	Nad
	pm	Nad
	74 am	Nad
	pm	Nad
	75 am	Nad
	pm	Nad
	76 am	Nad
	pm	Nad
	77 am	Nad
	pm	Nad
	78 am	Loose faeces.
	pm	Loose faeces.
	79 am	Nad
	pm	Nad
	80 am	Loose faeces.
	pm	Loose faeces.
	81 am	Nad
	pm	Nad
	82 am	Nad
	pm	Nad
	83 am	Nad
	pm	Nad
	84 am	Nad
	pm	Nad
	85 am	Nad
	pm	Nad
	86 am	Nad
	pm	Nad
	87 am	Nad
	pm	Nad
	88 am	Nad
	pm	Nad
	89 am	Nad
	pm	Nad
	90 am	Nad
	pm	Nad
	91 am	Nad
	pm	Nad
	92 am	Nad
	pm	Nad
	93 am	Nad
	pm	Nad
	94 am	Nad
	pm	Nad
	95 am	Nad
	pm	Nad

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W280f (contd)	96 am	Nad
	pm	Nad
	97 am	Nad
	pm	Sacrificed.

APPENDIX 6

Clinical signs

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1).

Abbreviations

Nad No abnormalities detected

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X393m	1	am	Nad.
		pm	Quiet and huddled. Picking at tail.
	2	am	Nad
		pm	Loose faeces.
	3	am	Quiet, loose faeces.
		pm	Quiet, loose faeces.
	4	am	Quiet, loose faeces.
		pm	Quiet, loose faeces.
	5	am	Loose/normal faeces.
		pm	Loose/normal faeces.
	6	am	Quiet.
		pm	Loose faeces.
	7	am	Loose faeces.
		pm	Loose faeces.
	8	am	Quiet, loose faeces.
		pm	Quiet, loose faeces.
	9	am	Quiet, normal faeces.
		pm	Quiet.
	10	am	Quiet.
		pm	Quiet.
	11	am	Quiet.
		pm	Nad.
	12	am	Quiet.
		pm	Nad.
	13	am	Nad.
		pm	Nad.
	14	am	Nad.
		pm	Nad.
	15	am	Nad.
		pm	Nad.
	16	am	Nad.
		pm	Nad.
	17	am	Nad.
		pm	Nad.
	18	am	Nad.
		pm	Nad.
	19	am	Nad.
		pm	Nad.
	20	am	Nad.
		pm	Nad.
	21	am	Nad.
		pm	Nad.
	22	am	Nad.
		pm	Nad.
	23	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X393m (contd)	24	am	Nad.
		pm	Nad.
	25	am	Nad.
		pm	Nad.
	26	am	Nad.
		pm	Nad.
	27	am	Nad.
		pm	Nad.
	28	am	Nad.
		pm	Nad.
	29	am	Nad.
		pm	Nad.
	30	am	Nad.
		pm	Nad.
	31	am	Nad.
		pm	Nad.
	32	am	Nad.
		pm	Nad.
	33	am	Nad.
		pm	Nad.
	34	am	Nad.
		pm	Nad.
	35	am	Nad.
		pm	Nad.
	36	am	Nad.
		pm	Nad.
	37	am	Nad.
		pm	Nad.
	38	am	Nad.
		pm	Nad.
	39	am	Nad.
		pm	Nad.
	40	am	Nad.
		pm	Nad.
	41	am	Loose faeces
		pm	Nad.
	42	am	Nad.
		pm	Nad.
	43	am	Nad.
		pm	Nad.
	44	am	Nad.
		pm	Nad.
	45	am	Nad.
		pm	Nad.
	46	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	47	am	Purple coloured urine in tray.
		pm	Purple skin discolouration after xylenol orange dose.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X393m	48	am	Purple coloured urine in tray.
		pm	Purple coloured urine in tray.
	49	am	Nad.
		pm	Nad.
	50	am	Nad.
		pm	Nad.
	51	am	Nad.
		pm	Nad.
	52	am	Nad.
		pm	Nad.
	53	am	Nad.
		pm	Nad.
	54	am	Nad.
		pm	Nad.
	55	am	Nad.
		pm	Nad.
	56	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose, purple urine.
	57	am	Nad.
		pm	Purple skin discolouration and purple urine after xylenol orange dose.
	58	am	Purple coloured urine in tray.
		pm	Purple coloured urine and faeces in tray.
	59	am	Nad.
		pm	Purple coloured urine in tray.
	60	am	Nad.
		pm	Nad.
	61	am	Nad.
		pm	Nad.
	62	am	Nad.
		pm	Nad.
	63	am	Nad.
		pm	Sacrificed.
X397m	1	am	Nad.
		pm	Loose/liquid faeces.
	2	am	Loose faeces.
		pm	Quiet, loose faeces.
	3	am	Quiet but alert, loose faeces.
		pm	Quiet, huddled on perch, loose faeces.
	4	am	Quiet, loose faeces.
		pm	Quiet, loose faeces.
	5	am	Loose/normal faeces.
		pm	Loose/normal faeces.
	6	am	Loose faeces.
		pm	Loose faeces, blood in tray.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X397m (contd)	7	am	Loose faeces.
		pm	Huddled and quiet, loose faeces.
	8	am	Quiet, normal faeces.
		pm	Quiet.
	9	am	Quiet.
		pm	Quiet.
	10	am	Quiet.
		pm	Nad.
	11	am	Quiet.
		pm	Nad.
	12	am	Nad.
		pm	Nad.
	13	am	Nad.
		pm	Nad.
	14	am	Nad.
		pm	Nad.
	15	am	Nad.
		pm	Nad.
	16	am	Nad.
		pm	Nad.
	17	am	Nad.
		pm	Nad.
	18	am	Nad.
		pm	Nad.
	19	am	Nad.
		pm	Nad.
	20	am	Nad.
		pm	Nad.
	21	am	Nad.
		pm	Nad.
	22	am	Nad.
		pm	Nad.
	23	am	Nad.
		pm	Nad.
	24	am	Nad.
		pm	Nad.
	25	am	Nad.
		pm	Nad.
	26	am	Nad.
		pm	Nad.
	27	am	Nad.
		pm	Nad.
	28	am	Nad.
		pm	Nad.
	29	am	Nad.
		pm	Nad.
	30	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X397m (contd)	31	am	Nad.
		pm	Nad.
	32	am	Nad.
		pm	Nad.
	33	am	Nad.
		pm	Nad.
	34	am	Nad.
		pm	Nad.
	35	am	Nad.
		pm	Nad.
	36	am	Nad.
		pm	Nad.
	37	am	Nad.
		pm	Nad.
	38	am	Nad.
		pm	Nad.
	39	am	Nad.
		pm	Nad.
	40	am	Nad.
		pm	Nad.
	41	am	Loose faeces.
		pm	Nad.
	42	am	Nad.
		pm	Nad.
	43	am	Nad.
		pm	Nad.
	44	am	Nad.
		pm	Nad.
	45	am	Nad.
		pm	Nad.
	46	am	Loose faeces.
		pm	Purple skin discolouration after xylenol orange dose.
	47	am	Purple coloured urine in tray.
		pm	Purple skin discolouration after xylenol orange dose.
	48	am	Purple coloured urine in tray.
		pm	Purple coloured urine in tray.
	49	am	Nad.
		pm	Nad.
	50	am	Nad.
		pm	Nad.
	51	am	Nad.
		pm	Nad.
	52	am	Nad.
		pm	Nad.
	53	am	Nad.
		pm	Nad.
	54	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X397m (contd)	55	am	Nad.
		pm	Nad.
	56	am	Nad.
		pm	Purple skin discolouration and purple urine after xylenol orange dose.
	57	am	Nad.
		pm	Purple skin discolouration and purple urine after xylenol orange dose.
	58	am	Purple urine in tray.
		pm	Purple urine and faeces in tray.
	59	am	Nad.
		pm	Purple urine in tray.
	60	am	Nad.
		pm	Nad.
	61	am	Nad.
		pm	Nad.
	62	am	Nad.
		pm	Nad.
	63	am	Nad.
		pm	Sacrificed.
X401m	1	am	Nad.
		pm	Quiet.
	2	am	Nad.
		pm	Loose faeces.
	3	am	Quiet, loose faeces.
		pm	Quiet, loose faeces.
	4	am	Quiet, loose faeces.
		pm	Quiet, loose faeces.
	5	am	Loose faeces.
		pm	Normal faeces.
	6	am	Loose faeces.
		pm	Loose/normal faeces.
	7	am	Loose faeces.
		pm	Loose faeces.
	8	am	Quiet, normal faeces.
		pm	Quiet.
	9	am	Quiet.
		pm	Quiet.
	10	am	Quiet.
		pm	Nad.
	11	am	Quiet.
		pm	Nad.
	12	am	Quiet.
		pm	Nad.
	13	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X401m (contd)	14	am	Nad.
		pm	Nad.
	15	am	Nad.
		pm	Quiet and huddled. Blood in tray from wound.
	16	am	Quiet.
		pm	Quiet.
	17	am	Nad.
		pm	Nad.
	18	am	Nad.
		pm	Nad.
	19	am	Nad.
		pm	Nad.
	20	am	Nad.
		pm	Nad.
	21	am	Nad.
		pm	Nad.
	22	am	Nad.
		pm	Nad.
	23	am	Nad.
		pm	Nad.
	24	am	Nad.
		pm	Nad.
	25	am	Nad.
		pm	Nad.
	26	am	Nad.
		pm	Nad.
	27	am	Nad.
		pm	Nad.
	28	am	Nad.
		pm	Nad.
	29	am	Loose faeces.
		pm	Nad.
	30	am	Nad.
		pm	Nad.
	31	am	Nad.
		pm	Nad.
	32	am	Nad.
		pm	Nad.
	33	am	Nad.
		pm	Nad.
	34	am	Nad.
		pm	Nad.
	35	am	Nad.
		pm	Nad.
	36	am	Nad.
		pm	Nad.
	37	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X401m (contd)	38	am	Nad.
		pm	Nad.
	39	am	Nad.
		pm	Nad.
	40	am	Nad.
		pm	Nad.
	41	am	Nad.
		pm	Nad.
	42	am	Nad.
		pm	Nad.
	43	am	Loose faeces.
		pm	Loose faeces.
	44	am	Normal faeces.
		pm	Nad.
	45	am	Nad.
		pm	Nad.
	46	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	47	am	Purple coloured urine in tray.
		pm	Purple skin discolouration after xylenol orange dose.
	48	am	Purple coloured urine in tray.
		pm	Purple coloured urine in tray.
	49	am	Liquid faeces.
		pm	Nad.
	50	am	Nad.
		pm	Nad.
	51	am	Nad.
		pm	Nad.
	52	am	Nad.
		pm	Nad.
	53	am	Nad.
		pm	Nad.
	54	am	Nad.
		pm	Nad.
	55	am	Nad.
		pm	Nad.
	56	am	Nad.
		pm	Purple skin and urine discolouration after xylenol orange dose.
	57	am	Nad.
		pm	Purple skin and urine discolouration after xylenol orange dose.
	58	am	Purple urine in tray.
		pm	Purple urine and faeces in tray.
	59	am	Nad.
		pm	Nad.
	60	am	Nad.
		pm	Nad.
	61	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X401m (contd)	62	am	Nad.
		pm	Nad.
	63	am	Nad.
		pm	Sacrificed.
X403m	1	am	Nad.
		pm	Nad.
	2	am	Nad.
		pm	Loose faeces.
	3	am	Loose faeces.
		pm	Quiet, loose faeces.
	4	am	Quiet, loose faeces.
		pm	Quiet, loose faeces.
	5	am	Nad.
		pm	Loose faeces.
	6	am	Loose faeces.
		pm	Loose faeces.
	7	am	Loose faeces.
		pm	Loose faeces.
	8	am	Quiet, normal faeces.
		pm	Quiet.
	9	am	Quiet.
		pm	Quiet.
	10	am	Quiet.
		pm	Nad.
	11	am	Quiet.
		pm	Nad.
	12	am	Quiet.
		pm	Nad.
	13	am	Nad.
		pm	Nad.
	14	am	Nad.
		pm	Nad.
	15	am	Nad.
		pm	Quiet.
	16	am	Nad.
		pm	Nad.
	17	am	Nad.
		pm	Nad.
	18	am	Nad.
		pm	Nad.
	19	am	Nad.
		pm	Nad.
	20	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X403m (contd)	21	am	Nad.
		pm	Nad.
	22	am	Nad.
		pm	Nad.
	23	am	Nad.
		pm	Nad.
	24	am	Nad.
		pm	Nad.
	25	am	Nad.
		pm	Nad.
	26	am	Nad.
		pm	Nad.
	27	am	Nad.
		pm	Nad.
	28	am	Nad.
		pm	Nad.
	29	am	Loose faeces.
		pm	Nad.
	30	am	Nad.
		pm	Nad.
	31	am	Nad.
		pm	Nad.
	32	am	Nad.
		pm	Nad.
	33	am	Nad.
		pm	Nad.
	34	am	Nad.
		pm	Nad.
	35	am	Nad.
		pm	Nad.
	36	am	Nad.
		pm	Nad.
	37	am	Nad.
		pm	Nad.
	38	am	Nad.
		pm	Nad.
	39	am	Nad.
		pm	Nad.
	40	am	Nad.
		pm	Nad.
	41	am	Nad.
		pm	Nad.
	42	am	Nad.
		pm	Nad.
	43	am	Loose faeces.
		pm	Loose faeces.
	44	am	Normal faeces.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X403m (contd)	45	am	Nad.
		pm	Nad.
	46	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	47	am	Purple urine in tray.
		pm	Purple skin discolouration after xylenol orange dose.
	48	am	Purple urine in tray.
		pm	Purple urine in tray.
	49	am	Liquid faeces.
		pm	Nad.
	50	am	Nad.
		pm	Nad.
	51	am	Nad.
		pm	Nad.
	52	am	Nad.
		pm	Nad.
	53	am	Dry scab on scrotum.
		pm	Nad.
	54	am	Nad.
		pm	Nad.
	55	am	Nad.
		pm	Nad.
	56	am	Nad.
		pm	Purple skin and urine discolouration after xylenol orange dose.
	57	am	Nad.
		pm	Purple skin and urine discolouration after xylenol orange dose.
	58	am	Purple urine in tray.
		pm	Purple urine and faeces in tray.
	59	am	Nad.
		pm	Nad.
	60	am	Nad.
		pm	Nad.
	61	am	Nad.
		pm	Nad.
	62	am	Nad.
		pm	Nad.
	63	am	Nad.
		pm	Sacrificed.
X398f	1	am	Nad.
		pm	Nad.
	2	am	Nad.
		pm	Loose faeces.
	3	am	Quiet. No faeces seen.
		pm	Loose faeces and mucus passed.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X398f (contd)	4	am	Quiet, loose faeces.
		pm	Quiet, normal faeces.
	5	am	Nad.
		pm	Nad.
	6	am	Nad.
		pm	Nad.
	7	am	Nad.
		pm	Nad.
	8	am	Quiet.
		pm	Nad.
	9	am	Quiet.
		pm	Quiet.
	10	am	Quiet.
		pm	Nad.
	11	am	Quiet.
		pm	Nad.
	12	am	Quiet.
		pm	Nad.
	13	am	Nad.
		pm	Nad.
	14	am	Nad.
		pm	Nad.
	15	am	Nad.
		pm	Nad.
	16	am	Nad.
		pm	Nad.
	17	am	Nad.
		pm	Nad.
	18	am	Nad.
		pm	Nad.
	19	am	Nad.
		pm	Nad.
	20	am	Nad.
		pm	Nad.
	21	am	Nad.
		pm	Nad.
	22	am	Loose faeces.
		pm	Loose faeces.
	23	am	Nad.
		pm	Nad.
	24	am	Liquid faeces.
		pm	Liquid faeces.
	25	am	Nad.
		pm	Nad.
	26	am	Nad.
		pm	Nad.
	27	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X398f (contd)	28	am	Nad.
		pm	Nad.
	29	am	Loose faeces.
		pm	Nad.
	30	am	Nad.
		pm	Nad.
	31	am	Nad.
		pm	Nad.
	32	am	Nad.
		pm	Nad.
	33	am	Nad.
		pm	Nad.
	34	am	Loose faeces.
		pm	Nad.
	35	am	Nad.
		pm	Nad.
	36	am	Nad.
		pm	Nad.
	37	am	Nad.
		pm	Nad.
	38	am	Nad.
		pm	Nad.
	39	am	Nad.
		pm	Nad.
	40	am	Nad.
		pm	Nad.
	41	am	Nad.
		pm	Nad.
	42	am	Nad.
		pm	Nad.
	43	am	Nad.
		pm	Nad.
	44	am	Loose faeces.
		pm	Loose faeces.
	45	am	Nad.
		pm	Nad.
	46	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	47	am	Purple urine in tray.
		pm	Purple skin discolouration after xylenol orange dose.
	48	am	Purple urine in tray.
		pm	Purple urine in tray.
	49	am	Liquid faeces.
		pm	Liquid faeces.
	50	am	Liquid faeces.
		pm	Loose faeces.
	51	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X398f (contd)	52	am	Nad.
		pm	Nad.
	53	am	Nad.
		pm	Nad.
	54	am	Nad.
		pm	Nad.
	55	am	Nad.
		pm	Nad.
	56	am	Nad.
		pm	Purple skin and urine discolouration after xylenol orange dose.
	57	am	Nad.
		pm	Purple skin and urine discolouration after xylenol orange dose.
	58	am	Purple urine in tray.
		pm	Purple urine and faeces in tray.
	59	am	Nad.
		pm	Nad.
	60	am	Nad.
		pm	Nad.
	61	am	Nad.
		pm	Nad.
	62	am	Nad.
		pm	Nad.
	63	am	Nad.
		pm	Sacrificed.
X402f	1	am	Nad.
		pm	Nad.
	2	am	Nad.
		pm	Nad.
	3	am	Nad.
		pm	Quiet.
	4	am	Quiet, loose faeces.
		pm	Quiet, loose faeces.
	5	am	Quiet but alert, normal faeces.
		pm	Quiet but alert, normal faeces.
	6	am	Nad.
		pm	Nad.
	7	am	Nad.
		pm	Nad.
	8	am	Nad.
		pm	Nad.
	9	am	Quiet.
		pm	Quiet.
	10	am	Quiet.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X402f (contd)	11	am	Quiet.
		pm	Nad.
	12	am	Quiet.
		pm	Nad..
	13	am	Quiet.
		pm	Quiet.
	14	am	Nad.
		pm	Nad.
	15	am	Nad.
		pm	Nad.
	16	am	Nad.
		pm	Nad.
	17	am	Nad.
		pm	Nad.
	18	am	Nad.
		pm	Loose faeces.
	19	am	Nad.
		pm	Nad.
	20	am	Loose faeces.
		pm	Loose faeces.
	21	am	Nad.
		pm	Nad.
	22	am	Nad.
		pm	Nad.
	23	am	Nad.
		pm	Nad.
	24	am	Nad.
		pm	Nad.
	25	am	Nad.
		pm	Nad.
	26	am	Nad.
		pm	Nad.
	27	am	Nad.
		pm	Nad.
	28	am	Nad.
		pm	Nad.
	29	am	Loose faeces.
		pm	Loose faeces.
	30	am	Loose faeces.
		pm	Nad.
	31	am	Loose faeces.
		pm	Loose faeces.
	32	am	Nad.
		pm	Nad.
	33	am	Nad.
		pm	Nad.
	34	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X402f (contd)	35	am	Nad.
		pm	Nad.
	36	am	Nad.
		pm	Nad.
	37	am	Nad.
		pm	Nad.
	38	am	Nad.
		pm	Nad.
	39	am	Nad.
		pm	Nad.
	40	am	Nad.
		pm	Nad.
	41	am	Nad.
		pm	Nad.
	42	am	Nad.
		pm	Nad.
	43	am	Nad.
		pm	Nad.
	44	am	Nad.
		pm	Nad.
	45	am	Nad.
		pm	Nad.
	46	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	47	am	Purple urine in tray.
		pm	Purple skin discolouration after xylenol orange dose.
	48	am	Purple urine in tray.
		pm	Purple urine in tray.
	49	am	Nad.
		pm	Nad.
	50	am	Nad.
		pm	Nad.
	51	am	Nad.
		pm	Nad.
	52	am	Nad.
		pm	Nad.
	53	am	Nad.
		pm	Nad.
	54	am	Nad.
		pm	Nad.
	55	am	Nad.
		pm	Nad.
	56	am	Nad.
		pm	Purple skin and urine discolouration after xylenol orange dose.
	57	am	Nad.
		pm	Purple skin and urine discolouration after xylenol orange dose.
	58	am	Purple urine in tray.
		pm	Purple urine and faeces in tray.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X402f (contd)	59	am	Purple urine in tray.
		pm	Nad.
	60	am	Sacrificed.
X406f	1	am	Nad.
		pm	Nad.
	2	am	Nad.
		pm	Loose faeces.
	3	am	Quiet, loose faeces.
		pm	Quiet, loose faeces.
	4	am	Quiet, loose faeces.
		pm	Quiet, loose faeces.
	5	am	Quiet.
		pm	Quiet.
	6	am	Nad.
		pm	Blood in tray.
	7	am	Quiet.
		pm	Quiet.
	8	am	Quiet.
		pm	Loose faeces, quiet.
	9	am	Quiet, normal faeces.
		pm	Quiet.
	10	am	Quiet.
		pm	Nad.
	11	am	Quiet.
		pm	Nad.
	12	am	Quiet.
		pm	Nad.
	13	am	Quiet.
		pm	Quiet.
	14	am	Nad.
		pm	Nad.
	15	am	Nad.
		pm	Nad.
	16	am	Nad.
		pm	Quiet and huddled.
	17	am	Quiet.
		pm	Nad.
	18	am	Nad.
		pm	Nad.
	19	am	Nad.
		pm	Nad.
	20	am	Loose faeces.
		pm	Loose faeces.
	21	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X406f (contd)	22	am	Nad.
		pm	Nad.
	23	am	Nad.
		pm	Nad.
	24	am	Nad.
		pm	Nad.
	25	am	Nad.
		pm	Nad.
	26	am	Nad.
		pm	Nad.
	27	am	Nad.
		pm	Nad.
	28	am	Nad.
		pm	Nad.
	29	am	Loose faeces.
		pm	Loose faeces.
	30	am	Loose faeces.
		pm	Nad.
	31	am	Nad.
		pm	Loose/normal faeces.
	32	am	Nad.
		pm	Nad.
	33	am	Nad.
		pm	Nad.
	34	am	Nad.
		pm	Nad.
	35	am	Nad.
		pm	Nad.
	36	am	Nad.
		pm	Nad.
	37	am	Nad.
		pm	Nad.
	38	am	Nad.
		pm	Nad.
	39	am	Nad.
		pm	Nad.
	40	am	Nad.
		pm	Nad.
	41	am	Nad.
		pm	Nad.
	42	am	Nad.
		pm	Nad.
	43	am	Nad.
		pm	Nad.
	44	am	Nad.
		pm	Nad.
	45	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X406f (contd)	46	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	47	am	Purple urine in tray.
		pm	Purple skin discolouration after xylenol orange dose.
	48	am	Purple urine and faeces in tray.
		pm	Purple urine and faeces in tray.
	49	am	Nad.
		pm	Liquid faeces.
	50	am	Nad.
		pm	Nad.
	51	am	Nad.
		pm	Nad.
	52	am	Nad.
		pm	Nad.
	53	am	Nad.
		pm	Nad.
	54	am	Nad.
		pm	Nad.
	55	am	Nad.
		pm	Nad.
	56	am	Nad.
		pm	Purple skin and urine discolouration after xylenol orange dose.
	57	am	Nad.
		pm	Purple skin and urine discolouration after xylenol orange dose.
	58	am	Purple urine in tray.
		pm	Purple urine and faeces in tray.
	59	am	Purple urine in tray.
		pm	Nad.
	60	am	Nad. Sacrificed.
X407f	1	am	Nad.
		pm	Nad.
	2	am	Nad.
		pm	Nad.
	3	am	Quiet, loose faeces.
		pm	Quiet, loose faeces.
	4	am	Quiet, loose faeces.
		pm	Quiet, loose faeces.
	5	am	Normal faeces.
		pm	Piloerection.
	6	am	Nad.
		pm	Nad.
	7	am	Nad.
		pm	Nad.
	8	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X407f (contd)	9	am	Quiet.
		pm	Quiet.
	10	am	Quiet.
		pm	Nad.
	11	am	Quiet.
		pm	Nad.
	12	am	Nad.
		pm	Nad.
	13	am	Nad.
		pm	Nad.
	14	am	Nad.
		pm	Nad.
	15	am	Nad.
		pm	Nad.
	16	am	Nad.
		pm	Piloerection.
	17	am	Nad.
		pm	Nad.
	18	am	Nad.
		pm	Nad.
	19	am	Nad.
		pm	Nad.
	20	am	Nad.
		pm	Nad.
	21	am	Nad.
		pm	Nad.
	22	am	Loose faeces.
		pm	Loose faeces.
	23	am	Nad.
		pm	Nad.
	24	am	Liquid faeces.
		pm	Liquid faeces.
	25	am	Nad.
		pm	Nad.
	26	am	Nad.
		pm	Nad.
	27	am	Nad.
		pm	Nad.
	28	am	Nad.
		pm	Nad.
	29	am	Loose faeces.
		pm	Nad.
	30	am	Nad.
		pm	Nad.
	31	am	Nad.
		pm	Nad.
	32	am	Left upper eyelid slightly swollen.
		pm	Left upper eyelid slightly swollen.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X407f (contd)	33	am	Nad.
		pm	Nad.
	34	am	Nad.
		pm	Nad.
	35	am	Nad.
		pm	Nad.
	36	am	Nad.
		pm	Nad.
	37	am	Nad.
		pm	Nad.
	38	am	Nad.
		pm	Nad.
	39	am	Nad.
		pm	Nad.
	40	am	Nad.
		pm	Nad.
	41	am	Nad.
		pm	Nad.
	42	am	Nad.
		pm	Nad.
	43	am	Nad.
		pm	Nad.
	44	am	Loose faeces.
		pm	Loose faeces.
	45	am	Nad.
		pm	Nad.
	46	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	47	am	Purple urine in tray.
		pm	Purple skin discolouration after xylenol orange dose.
	48	am	Purple urine in tray.
		pm	Purple urine in tray.
	49	am	Liquid faeces.
		pm	Loose faeces.
	50	am	Loose faeces.
		pm	Loose faeces.
	51	am	Nad.
		pm	Nad.
	52	am	Nad.
		pm	Nad.
	53	am	Nad.
		pm	Nad.
	54	am	Nad.
		pm	Nad.
	55	am	Nad.
		pm	Nad.
	56	am	Nad.
		pm	Purple skin and urine discolouration after xylenol orange dose.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X407f (contd)	57	am	Nad.
		pm	Purple skin and urine discolouration after xylenol orange dose.
	58	am	Purple urine in tray.
		pm	Purple urine and faeces in tray.
	59	am	Nad.
		pm	Nad.
	60	am	Nad.
		pm	Nad.
	61	am	Nad.
		pm	Nad.
	62	am	Nad.
		pm	Nad.
	63	am	Nad.
		pm	Sacrificed.
X656f	1	am	Nad.
		pm	Nad.
	2	am	Quiet but alert.
		pm	Nad.
	3	am	Quiet.
		pm	Loose faeces, quiet.
	4	am	Quiet, normal faeces.
		pm	Quiet.
	5	am	Nad.
		pm	Nad.
	6	am	Nad.
		pm	Nad.
	7	am	Quiet.
		pm	Quiet.
	8	am	Quiet.
		pm	Nad.
	9	am	Quiet.
		pm	Quiet.
	10	am	Quiet.
		pm	Nad.
	11	am	Quiet.
		pm	Nad.
	12	am	Quiet.
		pm	Nad.
	13	am	Nad.
		pm	Nad.
	14	am	Nad.
		pm	Nad.
	15	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X656f (contd)	16	am	Nad.
		pm	Nad.
	17	am	Nad.
		pm	Nad.
	18	am	Nad.
		pm	Nad.
	19	am	Nad.
		pm	Nad.
	20	am	Nad.
		pm	Nad.
	21	am	Nad.
		pm	Nad.
	22	am	Loose faeces.
		pm	Loose faeces.
	23	am	Nad.
		pm	Nad.
	24	am	Liquid faeces.
		pm	Liquid faeces.
	25	am	Nad.
		pm	Nad.
	26	am	Nad.
		pm	Nad.
	27	am	Nad.
		pm	Nad.
	28	am	Nad.
		pm	Nad.
	29	am	Loose faeces.
		pm	Nad.
	30	am	Nad.
		pm	Nad.
	31	am	Nad.
		pm	Nad.
	32	am	Nad.
		pm	Nad.
	33	am	Nad.
		pm	Nad.
	34	am	Nad.
		pm	Nad.
	35	am	Nad.
		pm	Nad.
	36	am	Nad.
		pm	Nad.
	37	am	Nad.
		pm	Nad.
	38	am	Nad.
		pm	Nad.
	39	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X656f (contd)	40	am	Nad.
		pm	Nad.
	41	am	Nad.
		pm	Nad.
	42	am	Nad.
		pm	Nad.
	43	am	Nad.
		pm	Nad.
	44	am	Loose/normal faeces.
		pm	Nad.
	45	am	Nad.
		pm	Nad.
	46	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	47	am	Purple urine in tray.
		pm	Purple skin discolouration after xylenol orange dose.
	48	am	Purple urine in tray.
		pm	Purple urine in tray.
	49	am	Liquid faeces.
		pm	Loose faeces.
	50	am	Loose faeces.
		pm	Loose faeces.
	51	am	Nad.
		pm	Nad.
	52	am	Nad.
		pm	Nad.
	53	am	Nad.
		pm	Nad.
	54	am	Nad.
		pm	Nad.
	55	am	Nad.
		pm	Nad.
	56	am	Nad.
		pm	Purple skin and urine discolouration after xylenon orange dose.
	57	am	Nad.
		pm	Purple skin and urine discolouration after xylenol orange dose.
	58	am	Purple urine in tray.
		pm	Purple urine and faeces in tray.
	59	am	Nad.
		pm	Nad.
	60	am	Nad. Sacrificed.
X399m	1	am	Quiet but alert.
		pm	Nad.
	2	am	Loose faeces.
		pm	Loose faeces.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X399m (contd)	3	am	Loose faeces.
		pm	Nad.
	4	am	Loose faeces.
		pm	Loose faeces.
	5	am	Loose faeces.
		pm	Nad.
	6	am	Nad.
		pm	Nad.
	7	am	Nad.
		pm	Nad.
	8	am	Nad.
		pm	Nad.
	9	am	Nad.
		pm	Nad.
	10	am	Nad.
		pm	Nad.
	11	am	Nad.
		pm	Nad.
	12	am	Nad.
		pm	Nad.
	13	am	Nad.
		pm	Nad.
	14	am	Nad.
		pm	Nad.
	15	am	Nad.
		pm	Nad.
	16	am	Nad.
		pm	Bright green urine.
	17	am	Yellow/green urine in tray.
		pm	Nad.
	18	am	Nad.
		pm	Nad.
	19	am	Nad.
		pm	Nad.
	20	am	Nad.
		pm	Nad.
	21	am	Nad.
		pm	Nad.
	22	am	Nad.
		pm	Nad.
	23	am	Nad.
		pm	Nad.
	24	am	Nad.
		pm	Nad.
	25	am	Nad.
		pm	Nad.
	26	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X399m (contd)	27	am	Nad.
		pm	Nad.
	28	am	Nad.
		pm	Nad.
	29	am	Nad.
		pm	Nad.
	30	am	Nad.
		pm	Nad.
	31	am	Nad.
		pm	Nad.
	32	am	Nad.
		pm	Nad.
	33	am	Nad.
		pm	Nad.
	34	am	Nad.
		pm	Nad.
	35	am	Nad.
		pm	Nad.
	36	am	Nad.
		pm	Nad.
	37	am	Nad.
		pm	Nad.
	38	am	Nad.
		pm	Nad.
	39	am	Nad.
		pm	Nad.
	40	am	Nad.
		pm	Nad.
	41	am	Nad.
		pm	Nad.
	42	am	Nad.
		pm	Nad.
	43	am	Nad.
		pm	Nad.
	44	am	Nad.
		pm	Nad.
	45	am	Nad.
		pm	Nad.
	46	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	47	am	Purple urine in tray.
		pm	Purple skin discolouration after xylenol orange dose.
	48	am	Purple urine in tray.
		pm	Purple faeces in tray.
	49	am	Nad.
		pm	Nad.
	50	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X399m (contd)	51	am	Nad.
		pm	Nad.
	52	am	Nad.
		pm	Nad.
	53	am	Nad.
		pm	Nad.
	54	am	Nad.
		pm	Nad.
	55	am	Nad.
		pm	Nad.
	56	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	57	am	Purple skin discolouration after xylenol orange dose.
		pm	Purple urine and faeces in tray.
	58	am	Purple urine in tray.
		pm	Purple faeces in tray.
	59	am	Trace of purple urine in tray.
		pm	Nad.
	60	am	Nad.
		pm	Nad.
	61	am	Nad.
		pm	Nad.
	62	am	Nad.
		pm	Nad.
	63	am	Nad.
		pm	Nad.
	64	am	Nad.
		pm	Nad.
	65	am	Nad. Sacrificed.
X328f	1	am	Quiet, blood spots in cage and tray.
		pm	Quiet.
	2	am	Loose faeces.
		pm	Loose faeces.
	3	am	Loose faeces.
		pm	Loose faeces.
	4	am	Loose faeces.
		pm	Loose faeces.
	5	am	Loose faeces.
		pm	Nad.
	6	am	Nad.
		pm	Nad.
	7	am	Nad.
		pm	Nad.
	8	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X328f (contd)	9	am	Nad.
		pm	Nad.
	10	am	Nad.
		pm	Nad.
	11	am	Nad.
		pm	Nad.
	12	am	Nad.
		pm	Nad.
	13	am	Nad.
		pm	Nad.
	14	am	Nad.
		pm	Nad.
	15	am	Nad.
		pm	Nad.
	16	am	Nad.
		pm	Bright green stained urine.
	17	am	Yellow/green stain in tray.
		pm	Nad.
	18	am	Nad.
		pm	Nad.
	19	am	Nad.
		pm	Nad.
	20	am	Nad.
		pm	Nad.
	21	am	Nad.
		pm	Nad.
	22	am	Nad.
		pm	Nad.
	23	am	Loose faeces.
		pm	Nad.
	24	am	Nad.
		pm	Nad.
	25	am	Nad.
		pm	Nad.
	26	am	Nad.
		pm	Nad.
	27	am	Discoloured urine.
		pm	Nad.
	28	am	Nad.
		pm	Nad.
	29	am	Nad.
		pm	Nad.
	30	am	Nad.
		pm	Nad.
	31	am	Loose faeces.
		pm	Nad.
	32	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X328f (contd)	33	am	Nad.
		pm	Nad.
	34	am	Nad.
		pm	Nad.
	35	am	Nad.
		pm	Nad.
	36	am	Nad.
		pm	Nad.
	37	am	Nad.
		pm	Nad.
	38	am	Nad.
		pm	Nad.
	39	am	Nad.
		pm	Nad.
	40	am	Nad.
		pm	Nad.
	41	am	Nad.
		pm	Nad.
	42	am	Nad.
		pm	Nad.
	43	am	Nad.
		pm	Nad.
	44	am	Nad.
		pm	Nad.
	45	am	Nad.
		pm	Nad.
	46	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	47	am	Purple urine in tray.
		pm	Purple skin discolouration after xylenol orange dose.
	48	am	Purple urine in tray.
		pm	Purple faeces in tray.
	49	am	Loose/liquid faeces.
		pm	Normal faeces.
	50	am	Nad.
		pm	Nad.
	51	am	Nad.
		pm	Nad.
	52	am	Nad.
		pm	Nad.
	53	am	Nad.
		pm	Nad.
	54	am	Nad.
		pm	Nad.
	55	am	Nad.
		pm	Nad.
	56	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X328f (contd)	57	am	Purple skin discolouration after xylenol orange dose.
		pm	Purple urine and faeces in tray.
	58	am	Purple urine in tray.
		pm	Purple faeces in tray.
	59	am	Trace of purple urine in tray.
		pm	Nad.
	60	am	Nad.
		pm	Nad.
	61	am	Nad.
		pm	Nad.
	62	am	Nad.
		pm	Nad.
	63	am	Nad.
		pm	Nad.
	64	am	Nad.
		pm	Nad.
	65	am	Nad. Sacrificed.
X394f	1	am	Alert and active.
		pm	Nad.
	2	am	Loose faeces.
		pm	Loose faeces.
	3	am	Loose faeces.
		pm	Loose faeces.
	4	am	Loose faeces.
		pm	Loose faeces.
	5	am	Loose faeces.
		pm	Nad.
	6	am	Dark/loose faeces.
		pm	Nad.
	7	am	Loose faeces.
		pm	Loose faeces.
	8	am	Nad.
		pm	Nad.
	9	am	Nad.
		pm	Nad.
	10	am	Nad.
		pm	Nad.
	11	am	Nad.
		pm	Nad.
	12	am	Nad.
		pm	Nad.
	13	am	Nad.
		pm	Nad.
	14	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X394f (contd)	15	am	Nad.
		pm	Nad.
	16	am	Nad.
		pm	Bright green stained urine.
	17	am	Yellow/green stain in tray.
		pm	Yellow/green stain in tray.
	18	am	Nad.
		pm	Nad.
	19	am	Nad.
		pm	Nad.
	20	am	Nad.
		pm	Nad.
	21	am	Nad.
		pm	Loose faeces.
	22	am	Nad.
		pm	Nad.
	23	am	Nad.
		pm	Nad.
	24	am	Nad.
		pm	Loose faeces.
	25	am	Normal faeces.
		pm	Nad.
	26	am	Nad.
		pm	Nad.
	27	am	Nad.
		pm	Nad.
	28	am	Nad.
		pm	Nad.
	29	am	Nad.
		pm	Nad.
	30	am	Nad.
		pm	Nad.
	31	am	Nad.
		pm	Nad.
	32	am	Nad.
		pm	Nad.
	33	am	Nad.
		pm	Nad.
	34	am	Nad.
		pm	Nad.
	35	am	Nad.
		pm	Nad.
	36	am	Nad.
		pm	Nad.
	37	am	Nad.
		pm	Nad.
	38	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X394f (contd)	39	am	Nad.
		pm	Nad.
	40	am	Nad.
		pm	Nad.
	41	am	Nad.
		pm	Nad.
	42	am	Nad.
		pm	Nad.
	43	am	Nad.
		pm	Nad.
	44	am	Nad.
		pm	Nad.
	45	am	Nad.
		pm	Nad.
	46	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	47	am	Purple urine in tray.
		pm	Purple skin discolouration after xylenol orange dose.
	48	am	Purple urine in tray.
		pm	Purple faeces in tray.
	49	am	Nad.
		pm	Nad.
	50	am	Nad.
		pm	Nad.
	51	am	Nad.
		pm	Nad.
	52	am	Nad.
		pm	Nad.
	53	am	Nad.
		pm	Nad.
	54	am	Nad.
		pm	Nad.
	55	am	Nad.
		pm	Nad.
	56	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	57	am	Purple skin discolouration after xylenol orange dose.
		pm	Purple urine and faeces in tray.
	58	am	Purple urine in tray.
		pm	Purple faeces in tray.
	59	am	Trace of purple urine in tray.
		pm	Nad.
	60	am	Nad.
		pm	Nad.
	61	am	Nad.
		pm	Nad.
	62	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X394f (contd)	63	am	Nad.
		pm	Nad.
	64	am	Nad.
		pm	Nad.
	65	am	Nad. Sacrificed.
X396f	1	am	Alert and active.
		pm	Nad.
	2	am	Loose faeces.
		pm	Nad.
	3	am	Loose faeces.
		pm	Nad.
	4	am	Loose faeces.
		pm	Loose/normal faeces.
	5	am	Loose faeces.
		pm	Nad.
	6	am	Piloerection.
		pm	Piloerection.
	7	am	Loose faeces.
		pm	Loose faeces.
	8	am	Nad.
		pm	Nad.
	9	am	Nad.
		pm	Nad.
	10	am	Nad.
		pm	Nad.
	11	am	Nad.
		pm	Nad.
	12	am	Nad.
		pm	Nad.
	13	am	Nad.
		pm	Nad.
	14	am	Nad.
		pm	Nad.
	15	am	Nad.
		pm	Nad.
	16	am	Nad.
		pm	Bright green urine.
	17	am	Yellow/green urine in tray.
		pm	Nad.
	18	am	Nad.
		pm	Nad.
	19	am	Nad.
		pm	Nad.
	20	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X396f (contd)	21	am	Nad.
		pm	Loose faeces.
	22	am	Nad.
		pm	Nad.
	23	am	Nad.
		pm	Nad.
	24	am	Nad.
		pm	Loose faeces.
	25	am	Normal faeces.
		pm	Nad.
	26	am	Nad.
		pm	Nad.
	27	am	Nad.
		pm	Nad.
	28	am	Nad.
		pm	Nad.
	29	am	Nad.
		pm	Nad.
	30	am	Nad.
		pm	Nad.
	31	am	Nad.
		pm	Nad.
	32	am	Nad.
		pm	Nad.
	33	am	Nad.
		pm	Nad.
	34	am	Nad.
		pm	Nad.
	35	am	Nad.
		pm	Nad.
	36	am	Nad.
		pm	Nad.
	37	am	Nad.
		pm	Nad.
	38	am	Nad.
		pm	Nad.
	39	am	Nad.
		pm	Nad.
	40	am	Nad.
		pm	Nad.
	41	am	Nad.
		pm	Nad.
	42	am	Nad.
		pm	Nad.
	43	am	Nad.
		pm	Nad.
	44	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X396f (contd)	45	am	Nad.
		pm	Nad.
	46	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	47	am	Purple urine in tray.
		pm	Purple skin discolouration after xylenol orange dose.
	48	am	Purple urine in tray.
		pm	Purple faeces in tray.
	49	am	Nad.
		pm	Nad.
	50	am	Nad.
		pm	Nad.
	51	am	Nad.
		pm	Nad.
	52	am	Nad.
		pm	Nad.
	53	am	Nad.
		pm	Nad.
	54	am	Nad.
		pm	Nad.
	55	am	Nad.
		pm	Nad.
	56	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	57	am	Purple skin discolouration after xylenol orange dose.
		pm	Purple urine and faeces in tray.
	58	am	Purple urine in tray.
		pm	Purple faeces in tray.
	59	am	Trace of purple urine in tray.
		pm	Nad.
	60	am	Nad.
		pm	Nad.
	61	am	Nad.
		pm	Nad.
	62	am	Nad.
		pm	Nad.
	63	am	Nad.
		pm	Nad.
	64	am	Nad.
		pm	Nad.
	65	am	Sacrificed.
X404f	1	am	Alert and active.
		pm	Nad.
	2	am	Nad.
		pm	Loose faeces.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X404f (contd)	3	am	Loose faeces.
		pm	Nad.
	4	am	Loose faeces.
		pm	Nad.
	5	am	Nad.
		pm	Nad.
	6	am	Nad.
		pm	Nad.
	7	am	Nad.
		pm	Nad.
	8	am	Nad.
		pm	Nad.
	9	am	Nad.
		pm	Nad.
	10	am	Nad.
		pm	Nad.
	11	am	Nad.
		pm	Nad.
	12	am	Nad.
		pm	Nad.
	13	am	Nad.
		pm	Nad.
	14	am	Nad.
		pm	Nad.
	15	am	Nad.
		pm	Nad.
	16	am	Nad.
		pm	Bright green urine.
	17	am	Yellow/green urine in tray.
		pm	Nad.
	18	am	Nad.
		pm	Nad.
	19	am	Nad.
		pm	Nad.
	20	am	Nad.
		pm	Nad.
	21	am	Nad.
		pm	Nad.
	22	am	Nad.
		pm	Loose faeces.
	23	am	Loose faeces.
		pm	Nad.
	24	am	Nad.
		pm	Nad.
	25	am	Nad.
		pm	Nad.
	26	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X404f (contd)	27	am	Discoloured urine.
		pm	Nad.
	28	am	Nad.
		pm	Nad.
	29	am	Nad.
		pm	Nad.
	30	am	Nad.
		pm	Nad.
	31	am	Nad.
		pm	Nad.
	32	am	Nad.
		pm	Nad.
	33	am	Nad.
		pm	Nad.
	34	am	Nad.
		pm	Nad.
	35	am	Nad.
		pm	Nad.
	36	am	Nad.
		pm	Nad.
	37	am	Nad.
		pm	Nad.
	38	am	Nad.
		pm	Nad.
	39	am	Nad.
		pm	Nad.
	40	am	Nad.
		pm	Nad.
	41	am	Nad.
		pm	Nad.
	42	am	Nad.
		pm	Nad.
	43	am	Nad.
		pm	Nad.
	44	am	Nad.
		pm	Nad.
	45	am	Nad.
		pm	Nad.
	46	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	47	am	Purple urine in tray.
		pm	Purple skin discolouration after xylenol orange dose.
	48	am	Purple urine in tray.
		pm	Purple faeces in tray.
	49	am	Nad.
		pm	Nad.
	50	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X404f (contd)	51	am	Nad.
		pm	Nad.
	52	am	Nad.
		pm	Nad.
	53	am	Nad.
		pm	Nad.
	54	am	Nad.
		pm	Nad.
	55	am	Nad.
		pm	Nad.
	56	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	57	am	Purple skin discolouration after xylenol orange dose.
		pm	Purple urine and faeces in tray.
	58	am	Purple urine in tray.
		pm	Purple faeces in tray.
	59	am	Trace of purple urine in tray.
		pm	Nad.
	60	am	Nad.
		pm	Nad.
	61	am	Nad.
		pm	Nad.
	62	am	Nad.
		pm	Nad.
	63	am	Nad.
		pm	Nad.
	64	am	Nad.
		pm	Nad.
	65	am	Nad.
		pm	Sacrificed.
X653f	1	am	Alert and active.
		pm	Nad.
	2	am	Loose faeces.
		pm	Nad.
	3	am	Loose faeces
		pm	Nad.
	4	am	Loose faeces.
		pm	Loose faeces.
	5	am	Loose faeces.
		pm	Nad.
	6	am	Loose faeces.
		pm	Loose faeces.
	7	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X653f (contd)	8	am	Nad.
		pm	Nad.
	9	am	Nad.
		pm	Nad.
	10	am	Nad.
		pm	Nad.
	11	am	Nad.
		pm	Nad.
	12	am	Nad.
		pm	Nad.
	13	am	Nad.
		pm	Nad.
	14	am	Nad.
		pm	Nad.
	15	am	Nad.
		pm	Nad.
	16	am	Nad.
		pm	Bright green urine.
	17	am	Yellow/green urine in tray.
		pm	Nad.
	18	am	Nad.
		pm	Nad.
	19	am	Nad.
		pm	Nad.
	20	am	Nad.
		pm	Nad.
	21	am	Nad.
		pm	Nad.
	22	am	Nad.
		pm	Nad.
	23	am	Nad.
		pm	Nad.
	24	am	Nad.
		pm	Nad.
	25	am	Nad.
		pm	Nad.
	26	am	Nad.
		pm	Nad.
	27	am	Nad.
		pm	Nad.
	28	am	Nad.
		pm	Nad.
	29	am	Nad.
		pm	Nad.
	30	am	Nad.
		pm	Nad.
	31	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X653f (contd)	32	am	Nad.
		pm	Nad.
	33	am	Nad.
		pm	Nad.
	34	am	Nad.
		pm	Nad.
	35	am	Nad.
		pm	Nad.
	36	am	Nad.
		pm	Nad.
	37	am	Nad.
		pm	Nad.
	38	am	Nad.
		pm	Nad.
	39	am	Nad.
		pm	Nad.
	40	am	Nad.
		pm	Nad.
	41	am	Nad.
		pm	Nad.
	42	am	Nad.
		pm	Nad.
	43	am	Nad.
		pm	Nad.
	44	am	Nad.
		pm	Nad.
	45	am	Nad.
		pm	Nad.
	46	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	47	am	Purple urine in tray.
		pm	Purple skin discolouration after xylenol orange dose.
	48	am	Purple urine in tray.
		pm	Purple faeces in tray.
	49	am	Nad.
		pm	Nad.
	50	am	Nad.
		pm	Nad.
	51	am	Nad.
		pm	Nad.
	52	am	Nad.
		pm	Nad.
	53	am	Nad.
		pm	Nad.
	54	am	Nad.
		pm	Nad.
	55	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X653f (contd)	56	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	57	am	Purple skin discolouration after xylenol orange dose.
		pm	Purple urine and faeces in tray.
	58	am	Purple urine in tray.
		pm	Purple faeces in tray.
	59	am	Purple urine and dark faeces in tray.
		pm	Nad.
	60	am	Nad.
		pm	Nad.
	61	am	Nad.
		pm	Nad.
	62	am	Nad.
		pm	Nad.
	63	am	Nad.
		pm	Nad.
	64	am	Nad.
		pm	Nad.
	65	am	Nad.
		pm	Sacrificed.
X654f	1	am	Quiet but alert. Large amount of blood in tray.
		pm	Quiet but alert.
	2	am	Nad.
		pm	Loose faeces.
	3	am	Loose faeces.
		pm	Nad.
	4	am	Loose faeces.
		pm	Loose faeces.
	5	am	Loose faeces.
		pm	Nad.
	6	am	Loose faeces.
		pm	Nad.
	7	am	Quiet.
		pm	Nad.
	8	am	Nad.
		pm	Nad.
	9	am	Nad.
		pm	Nad.
	10	am	Nad.
		pm	Nad.
	11	am	Nad.
		pm	Nad.
	12	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X654f (contd)	13	am	Nad.
		pm	Nad.
	14	am	Nad.
		pm	Nad.
	15	am	Nad.
		pm	Nad.
	16	am	Nad.
		pm	Bright green urine.
	17	am	Yellow/green urine in tray.
		pm	Nad.
	18	am	Nad.
		pm	Nad.
	19	am	Nad.
		pm	Nad.
	20	am	Nad.
		pm	Nad.
	21	am	Nad.
		pm	Nad.
	22	am	Nad.
		pm	Nad.
	23	am	Nad.
		pm	Nad.
	24	am	Nad.
		pm	Nad.
	25	am	Nad.
		pm	Nad.
	26	am	Nad.
		pm	Nad.
	27	am	Nad.
		pm	Nad.
	28	am	Nad.
		pm	Nad.
	29	am	Nad.
		pm	Nad.
	30	am	Nad.
		pm	Nad.
	31	am	Nad.
		pm	Nad.
	32	am	Nad.
		pm	Nad.
	33	am	Nad.
		pm	Nad.
	34	am	Nad.
		pm	Nad.
	35	am	Nad.
		pm	Nad.
	36	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X654f (contd)	37	am	Nad.
		pm	Nad.
	38	am	Nad.
		pm	Nad.
	39	am	Nad.
		pm	Nad.
	40	am	Nad.
		pm	Nad.
	41	am	Nad.
		pm	Nad.
	42	am	Nad.
		pm	Nad.
	43	am	Nad.
		pm	Nad.
	44	am	Nad.
		pm	Nad.
	45	am	Nad.
		pm	Nad.
	46	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	47	am	Purple urine in tray.
		pm	Purple skin discolouration after xylenol orange dose.
	48	am	Purple urine in tray.
		pm	Purple faeces in tray.
	49	am	Nad.
		pm	Nad.
	50	am	Nad.
		pm	Nad.
	51	am	Nad.
		pm	Nad.
	52	am	Nad.
		pm	Nad.
	53	am	Nad.
		pm	Nad.
	54	am	Nad.
		pm	Nad.
	55	am	Nad.
		pm	Nad.
	56	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	57	am	Nad.
		pm	Purple urine and faeces in tray.
	58	am	Purple urine in tray.
		pm	Purple faeces in tray.
	59	am	Purple urine and dark faeces in tray.
		pm	Nad.
	60	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
X654f (contd)	61	am	Nad.
		pm	Nad.
	62	am	Nad.
		pm	Nad.
	63	am	Nad.
		pm	Nad.
	64	am	Nad.
		pm	Nad.
	65	am	Nad.
		pm	Sacrificed.
W684f	1	am	Alert and active.
		pm	Quiet.
	2	am	Nad.
		pm	Loose faeces.
	3	am	Loose faeces.
		pm	Nad.
	4	am	Loose faeces.
		pm	Loose faeces.
	5	am	Loose faeces.
		pm	Nad.
	6	am	Nad.
		pm	Nad.
	7	am	Nad.
		pm	Nad.
	8	am	Loose faeces.
		pm	Normal faeces.
	9	am	Nad.
		pm	Nad.
	10	am	Nad.
		pm	Nad.
	11	am	Nad.
		pm	Nad.
	12	am	Nad.
		pm	Nad.
	13	am	Nad.
		pm	Nad.
	14	am	Nad.
		pm	Nad.
	15	am	Nad.
		pm	Nad.
	16	am	Nad.
		pm	Bright green stained urine.
	17	am	Yellow/green stain in tray.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
W684f (contd)	18	am	Nad.
		pm	Nad.
	19	am	Nad.
		pm	Nad.
	20	am	Nad.
		pm	Nad.
	21	am	Nad.
		pm	Nad.
	22	am	Nad.
		pm	Nad.
	23	am	Nad.
		pm	Nad.
	24	am	Nad.
		pm	Nad.
	25	am	Nad.
		pm	Nad.
	26	am	Loose faeces.
		pm	Nad.
	27	am	Nad.
		pm	Nad.
	28	am	Nad.
		pm	Nad.
	29	am	Nad.
		pm	Nad.
	30	am	Nad.
		pm	Nad.
	31	am	Nad.
		pm	Nad.
	32	am	Nad.
		pm	Nad.
	33	am	Nad.
		pm	Nad.
	34	am	Nad.
		pm	Nad.
	35	am	Nad.
		pm	Nad.
	36	am	Nad.
		pm	Nad.
	37	am	Nad.
		pm	Nad.
	38	am	Nad.
		pm	Nad.
	39	am	Nad.
		pm	Nad.
	40	am	Nad.
		pm	Nad.
	41	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
W684f (contd)	42	am	Nad.
		pm	Nad.
	43	am	Nad.
		pm	Nad.
	44	am	Nad.
		pm	Nad.
	45	am	Nad.
		pm	Nad.
	46	am	Loose faeces.
		pm	Purple skin discolouration after xylenol orange dose.
	47	am	Purple urine in tray.
		pm	Purple skin discolouration after xylenol orange dose.
	48	am	Purple urine in tray.
		pm	Purple faeces in tray.
	49	am	Nad.
		pm	Nad.
	50	am	Loose faeces.
		pm	Loose faeces.
	51	am	Loose faeces.
		pm	Normal faeces.
	52	am	Loose faeces.
		pm	Loose faeces.
	53	am	Normal faeces.
		pm	Nad.
	54	am	Nad.
		pm	Nad.
	55	am	Nad.
		pm	Nad.
	56	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	57	am	Purple skin discolouration after xylenol orange dose.
		pm	Purple urine and faeces in tray.
	58	am	Purple urine in tray.
		pm	Purple faeces in tray.
	59	am	Trace of purple urine in tray.
		pm	Nad.
	60	am	Nad.
		pm	Nad.
	61	am	Nad.
		pm	Nad.
	62	am	Nad.
		pm	Nad.
	63	am	Nad.
		pm	Nad.
	64	am	Nad.
		pm	Nad.
	65	am	Nad.
		pm	Sacrificed.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
W702f	1	am	Alert and active.
		pm	Nad.
	2	am	Loose faeces.
		pm	Loose faeces.
	3	am	Loose faeces.
		pm	Nad.
	4	am	Nad.
		pm	Loose faeces.
	5	am	Nad.
		pm	Nad.
	6	am	Nad.
		pm	Nad.
	7	am	Nad.
		pm	Nad.
	8	am	Nad.
		pm	Nad.
	9	am	Nad.
		pm	Nad.
	10	am	Nad.
		pm	Nad.
	11	am	Nad.
		pm	Nad.
	12	am	Nad.
		pm	Nad.
	13	am	Nad.
		pm	Nad.
	14	am	Nad.
		pm	Nad.
	15	am	Nad.
		pm	Nad.
	16	am	Nad.
		pm	Bright green urine.
	17	am	Yellow/green urine in tray.
		pm	Nad.
	18	am	Nad.
		pm	Nad.
	19	am	Nad.
		pm	Nad.
	20	am	Nad.
		pm	Nad.
	21	am	Nad.
		pm	Nad.
	22	am	Nad.
		pm	Nad.
	23	am	Nad.
		pm	Nad.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
W702f (contd)	24	am	Nad.
		pm	Nad.
	25	am	Nad.
		pm	Nad.
	26	am	Loose faeces.
		pm	Nad.
	27	am	Nad.
		pm	Nad.
	28	am	Nad.
		pm	Nad.
	29	am	Nad.
		pm	Nad.
	30	am	Nad.
		pm	Nad.
	31	am	Nad.
		pm	Nad.
	32	am	Nad.
		pm	Nad.
	33	am	Nad.
		pm	Nad.
	34	am	Nad.
		pm	Nad.
	35	am	Nad.
		pm	Nad.
	36	am	Nad.
		pm	Nad.
	37	am	Nad.
		pm	Nad.
	38	am	Nad.
		pm	Nad.
	39	am	Nad.
		pm	Nad.
	40	am	Nad.
		pm	Nad.
	41	am	Nad.
		pm	Nad.
	42	am	Nad.
		pm	Nad.
	43	am	Nad.
		pm	Nad.
	44	am	Nad.
		pm	Nad.
	45	am	Nad.
		pm	Nad.
	46	am	Loose faeces.
		pm	Purple skin discolouration after xylenol orange dose.
	47	am	Purple urine in tray.
		pm	Purple skin discolouration after xylenol orange dose.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.		Clinical signs
W702f (contd)	48	am	Purple urine in tray.
		pm	Purple faeces in tray.
	49	am	Nad.
		pm	Nad.
	50	am	Loose faeces.
		pm	Loose faeces.
	51	am	Loose faeces.
		pm	Normal faeces.
	52	am	Loose faeces.
		pm	Loose faeces.
	53	am	Normal faeces.
		pm	Nad.
	54	am	Nad.
		pm	Nad.
	55	am	Nad.
		pm	Nad.
	56	am	Nad.
		pm	Purple skin discolouration after xylenol orange dose.
	57	am	Purple skin discolouration after xylenol orange dose.
		pm	Purple urine and faeces in tray.
	58	am	Purple urine in tray.
		pm	Purple faeces in tray.
	59	am	Trace of purple urine in tray.
		pm	Nad.
	60	am	Nad.
		pm	Nad.
	61	am	Nad.
		pm	Nad.
	62	am	Nad.
		pm	Nad.
	63	am	Nad.
		pm	Nad.
	64	am	Nad.
		pm	Nad.
	65	am	Nad.
		pm	Sacrificed.

EXPERIMENTAL PROCEDURE

ANIMAL SUPPLY

Donor animals

Transgenic piglets were selected from litters produced by the Sponsor under Project Licence No. PPL [redacted]. Transgenic piglets supplied for the study *ca* 4 - 6 weeks old and their weights were in the range 4.6 - 8.6 kg.

Recipient animals

Wild-caught baboons *(Papio anubis)* were obtained through a UK commercial supplier [redacted]. Their estimated age at transplant was 2 - 6 years and their weights in the range 6.7 - 9.3 kg.

The animals used in this study were selected from stock held on behalf of the Sponsor to undergo screening as suitable recipients. Based on the results of the prescreening investigations, animals were selected by the Sponsor for transplant (see **PRE-OPERATIVE INVESTIGATIONS**). Only data relating to those animals that underwent transplant is presented in this report.

ANIMAL MANAGEMENT

Piglets

On the day of transplant, selected animals were delivered to Huntingdon Life Sciences by the Sponsor.

Baboons

On arrival at Huntingdon Life Sciences all animals were examined by a Veterinary Officer, receive an intramuscular injection of [redacted] to eliminate possible tapeworm infestation and allocated a unique colony number, which will be tattooed under the right arm. Intrapalpebral tuberculin test will be performed soon after arrival, or at least 6 weeks after the last test performed by the supplier. Due to the frequency of planned laboratory investigations and by virtue of the fact that these animals will be immunosuppressed, intrapalebral tuberculin testing was stopped following transplant.

The animals were housed individually in cages specifically designed to house non-human primates in clean and secure conditions. The animals were housed in cages measuring 78 cm wide, 103 cm deep and 230 cm high. The cages were constructed of stainless steel framework and 'printboard' walls, shelves and ceiling, incorporating a squeeze-back system, food hopper, water bottle holder and a removable 2.5 x 2.5 cm grid floor. Under the front half of each cage was a removable tray which contained wood chippings (Gold Chips sawdust: [redacted]) for use as a litter/forage substrate. The cages were cleaned and litter replaced each day. Automatic drinking valves, for the supply of drinking water, were used and tested each day.

If considered appropriate, upon completion of the first week following transplant, animals were paired up with a non-transplanted animal. It is recognised that the pairing-up of animals may be beneficial to their continued post-operative recovery and long-term survival.

The rooms in which the animals were kept were as far as practicable isolated from external disturbances. The room temperature was maintained within the range 18 to 25°C, using heat exchangers connected to hot water supplied from oil-fuelled boilers. Relative humidity was maintained within the range 40 to 90%. The environment was governed by a computer-controlled building management system which continuously monitored the temperature and humidity controls and the operational state of the air handling plant. Temperature and relative humidity were recorded using a Rototherm Recorder. Deviations in temperature and/or relative humidity outside the set limits (20 - 26°C, 45 - 70% RH) were due to the use of fan heaters as supplementary heat sources and when water was used to wash down cages and/or floor. Artificial lighting was used and was controlled to give 12 hours of light and 12 hours of dark per 24 hours. Air extraction was *via* a balanced system designed to give fifteen air changes per hour.

FOOD AND WATER

Baboons were each offered 350 grams, of standard dry diet (Primate Diet: [redacted]), daily in the morning. In the morning, the residue of the previous day was removed and weighed. All animals were starved overnight prior to operation.

Water was available at all times and Vitamin C (Blackcurrant, [redacted]) and [redacted] (a Vitamin B_{12} preparation, [redacted]) were added to the drinking water on one day of each week.

There was no information available to the Study Director to indicate that any non-nutrient substance likely to influence the effect of the test substances could reasonably be expected to be present in the diet or the drinking water, both of which were routinely subjected to chemical analysis. Results of all the analyses were lodged in the Huntingdon Life Sciences Archives.

Wholemeal bread and fresh fruit or vegetable produce were offered in order to enrich the environment and improve the interaction between the animals and their handlers.

STUDY DESIGN

All animals were considered on an individual basis. A total of 10 male animals underwent orthotopic cardiac xenograft transplant. The Sponsor was responsible for categorising the reasons why animals were sacrificed.

All animals that underwent transplant received immunosuppressive treatment with a combination of [redacted]

Immunosuppressive treatment commenced on Day -1, the day of transplant being designated Day 0.

Details of donor-recipient pairings for transplants and the dates on which they were performed are listed in Appendix 1. All recipient animals were identified by their unique HRC colony number.

The study was designed such that all animals initially followed a standard immunosuppressive protocol prior to and immediately following transplant. After a few days the immunosuppressive regime was then individually tailored for each animal being based on the results of laboratory investigations and blood drug levels. The initial dosing regimes are summarised as follows:

[redacted] was initially administered as [redacted] administered by intramuscular injection on Days [redacted] and [redacted] at dosage levels of [redacted] and [redacted]. Oral administration of [redacted] commenced on Day [redacted] at a dosage level advised by the Sponsor and was given by gavage as a split dose morning and late afternoon.

[redacted] was administered by intravenous injection on Day [redacted] at a dosage level of [redacted] and on Day [redacted] at [redacted] or [redacted]. Administration was continued on Days [redacted] and [redacted] at a dosage of [redacted] and then discontinued

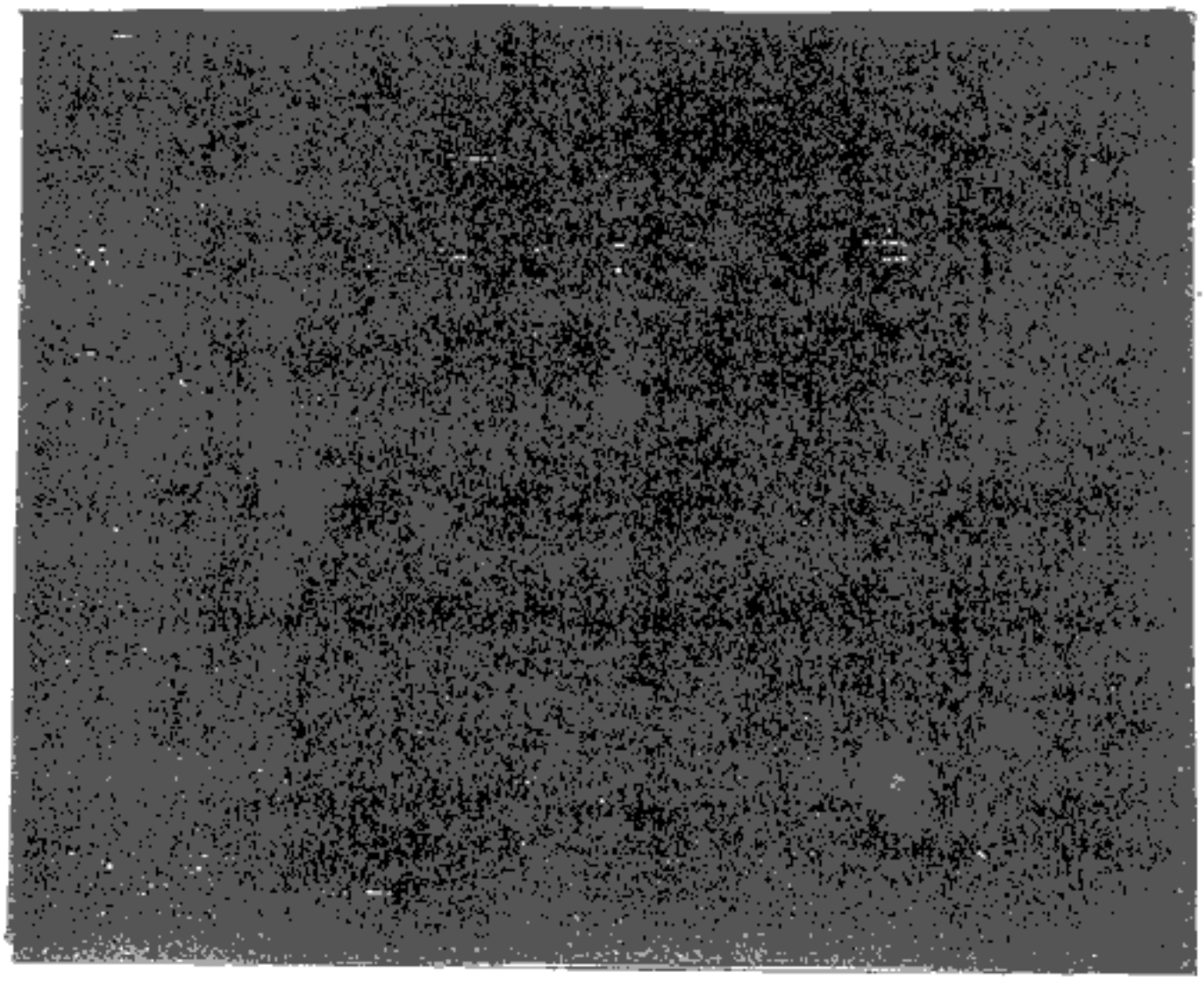
[redacted] was administered by intravenous injection at a dosage level of [redacted] at the time of transplant. Animals were dosed orally with [redacted] at the same dosage level on Days [redacted] and [redacted] after which the dosage level was reduced daily by [redacted] increments until a dosage of [redacted] was reached. Thereafter animals were maintained at that dosage level until advised otherwise by the Sponsor.

Details of the immunosuppressive regimes applied to individual animals are presented in Appendix 3.

Transplant operations were performed on 1 recipient animal per day and were spread over a period of several weeks, dependent on the availability of suitable donor animals. The commencement of the study for these subgroups was therefore varied dependent on when the transplant was performed.

The animals were housed in the [redacted]

PREPARATION OF THE IMMUNOSUPPRESSANT TREATMENTS



ADMINISTRATION OF THE IMMUNOSUPPRESSANT TREATMENTS

The animals were dosed at approximately the same time each morning and in the afternoon when applicable. Individual doses were adjusted daily according to the most recent bodyweight. The required quantity of each test solution was measured into a suitably graduated plastic syringe. For oral dosing the test solutions were administered through a plastic catheter [redacted] inserted *via* the mouth into the stomach. The catheter was flushed through with 5/10 ml of [redacted] (a high carbohydrate, low electrolyte, low fluid drink; [redacted]

For intravenous administration, the test solution was injected using a [redacted] infusion set inserted into the cephalic or saphenous vein.

For intramuscular administration, the test solution was injected through an appropriate gauge hypodermic needle. The animal was dosed in the thigh, the hair having been removed by clipping to facilitate administration and to observe any local reaction to the injection.

Intravenous administration of steroid on the day of transplant was carried out during surgery. The dose was administered through an indwelling cannula inserted into a peripheral vein.

PRE-OPERATIVE INVESTIGATIONS

During the acclimatisation period, blood samples were obtained from potential recipient animals for various investigations to enable the selection of the most compatible donor-recipient pairings. Blood samples were obtained for the following investigations.

Huntingdon Life Sciences

1. Pre-transplant haematology and biochemistry

Imutran Limited

1. Anti-pig antibody titres)
2. CH50) (9 ml into plain tubes)
3. Blood group)

Investigations carried out on donor animals were the responsibility of the Sponsor and, as such, have been documented and reported separately.

ORTHOTOPIC HEART XENOTRANSPLANTATION

NOTE:

Minor modifications to the following procedures may be employed at the discretion of the attending surgeon. As such, any deviations to these procedures were documented in the study records but unless considered major, were not detailed in a Protocol Amendment.

Anaesthesia and Monitoring

Donor operation

The donor animal was sedated with [redacted] administered by intramuscular injection at a dosage of [redacted]. Anaesthesia was induced with [redacted] in an [redacted] mixture, delivered via a face mask. Following transfer to the operating table, a tracheotomy was performed to allow endotracheal intubation, and mechanical ventilation will be commenced. The animal was maintained on a [redacted] mixture and [redacted] at a concentration of [redacted]

Recipient operation

The animal was fasted for 8 - 12 hours prior to surgery (overnight). While still within the animal holding area, the animal was given an intramuscular injection of [redacted] and [redacted]. Once sedated the animal was transferred to the operating suite. The thorax, neck, groin area and both limbs were shaved to allow intravenous and intra-arterial access. A cannula was inserted into the saphenous vein and an intravenous injection of [redacted] given. An endotracheal tube was inserted and the animal maintained on 0_2 with the addition of [redacted] at a concentration of [redacted] as necessary. [redacted] was also infused intravenously.

A catheter was inserted into the bladder and the end attached to a graduated collection container. A venous cannula was inserted for measurement of central venous pressure and a femoral artery cannula inserted for measurement of blood pressure and to obtain samples for blood pressure and to obtain samples for blood gas analysis.

Haematology and biochemistry measurements

Haematology:	act, Hb, PCV, platelets, total white cell counts, lymphocytes, neutrophils, antibody titre (anti-pig).
Biochemistry:	Arterial blood gases (pO_2, pCO_2), pH, H + Base excess, standard bicarbonate, potassium, sodium, chloride, ionised calcium, urea.

The measurements performed and the time of blood sampling were detailed in the study records.

Surgical procedure

Donor operation

A median sternotomy was performed and the pericardium opened longitudinally. A pulmonary artery catheter was inserted into the jugular vein or superior vena cava and cardiac output measurement made. The ascending aorta was dissected from the pulmonary artery to allow subsequent application of a cross-clamp. The superior vena cava (SVC) was mobilised at the level of the azygos to allow SVC ligation above the sinus node. Two ties were then placed around the SVC but not ligated at that stage, the inferior vena cava was mobilised.

The pig was fully heparinised [redacted]. A cardioplegia cannula was inserted in the ascending aorta. The SVC was doubly ligated and divided between the ligatures. The IVC was clamped at the level of the innominate artery and cardioplegia solution [redacted] at 4°C) saline was then poured over the heart to cool it rapidly.

The IVC was divided proximal to the clamp decompressing the right side for the heart, and the left inferior pulmonary vein was divided to decompress the left side of the heart. Infusion pressure in the aorta did not exceed more than 70 mmHg. During infusion the heart was gently massed on occasion to ensure that decompression was achieved. Cardioplegic infusion was usually completed within a few minutes. The topical saline was then sucked out of the pericardial cavity and section of the pulmonary veins was completed. The aorta was divided close to the cross-clamp and the pulmonary artery was then divided across the major right and left branches. The apex of the heart was then lifted and mediastinal tissue posterior to the atrium and major vessels were divided allowing the heart to be removed from the pericardial cavity.

Preparation of the donor heart

The heart was placed in a bowl of cold (4°C) saline during preparation for insertion into the recipient. The right atrial cavity was opened postero-laterally at the IVC orifice, continuing the incision into the base of the right atrial appendage avoiding the areas of the coronary sinus and the sinuatrial node. Tissue between the orifices of the four pulmonary veins on the posterior aspect of the left atrium were excised leaving one large opening. The aorta and pulmonary arteries were not trimmed until the atrial anastomoses had been completed. Simple defects as patent foramen ovale were repaired.

Recipient operation:

Institution of cardiopulmonary bypass

A median sternotomy was performed and the pericardium opened longitudinally. A pulmonary artery catheter was inserted into the jugular vein or superior vena cava and cardiac output measurement made. After heparinisation cardiopulmonary bypass was initiated *via* cannulae inserted into the ascending aorta at the level of the innominate artery and into the SVC and IVC *via* the lateral wall of the right atrium. Snares were placed around the IVC and SVC. Cooling to 28°C helped prevent early rewarming of the donor heart as it lay in the pericardial cavity during insertion. The aorta was then cross-clamped immediately proximal to the aortic cannula.

Excision of the recipient's heart

The heart was excised by dividing the right and left atrial walls close to the atrio-ventricular groove and the atrial septum, leaving a cuff of atrial wall to allow suture of the donor heart. Both atrial appendages were excised to prevent subsequent thrombus formulation. The aorta and main pulmonary artery were divided as close to their valves as possible. Subsequently these vessels were trimmed before being sutured to their counterparts in the donor heart.

Implantation of the donor heart

The donor heart was then placed over the left side of the divided sternum parallel to the remnant of the excised recipient heart. The free walls of both recipient and donor left atria then lay adjacent to each other. Using 4/0 or 5/0 prolene suture the left atrial walls were anastomosed by a continuous suture beginning at the base of the donor left atrial appendage and at a point close to the caudal end of the recipient left superior pulmonary vein. At a convenient stage the donor heart was drawn down into the pericardium and the suture tightened. The suturing was continued around the superior and inferior walls of the left atrium onto the atrial septum and the suture was then tied in the middle of the septum.

It was important to maintain myocardial temperatures as low as possible, preferable below 12°C through the ischaemic period and regular irrigations of the pericardial cavity were performed with cold saline.

The right atria was then anastomosed using a double-ended suture of 5/0 or 4/0 prolene. The suture was initially placed at the midpoint in the donor septum and at a convenient point the posterior lip of the incision in the recipient right atrium (usually caudal to the mid-point). The anastomosis was continued first inferiorly because of the small cuff of recipient right atrium that remains in the region of the IVC. The superior anastomosis was then completed and the ends of the sutures were tied at the midpoint onto the right free atrial wall. The two pulmonary arteries were then trimmed to their lengths and anastomosed by using a continuous suture of 4/0 or 5/0 PDS. The aorta was similarly trimmed and anastomosed by continuous suture of 4/0 or 5/0 PDS.

De-airing and cessation of cardiopulmonary bypass

Air needles were placed in the apex of the left ventricle, the anterior wall of the right ventricle, the ascending aorta and the main pulmonary artery. The SVC and IVC snares were released and the heart gently massaged to expel air from the ventricles and major vessels. The lungs were gently ventilated at that time to increase the venous return to the left side of the heart expressing further air, although care was taken to ensure that the heart was not overdistended. The aortic cross-clamp was released allowing the coronary arteries of the donor heart to be perfused again with oxygenated blood. Further efforts were made to expel air from both ventricles and major arteries at that time.

As total body rewarming occurred vigorous ventricular fibrillation or spontaneous co-ordinated myocardial contraction occurred. If ventricular fibrillation was present, defibrillation was attempted when the systemic temperature was greater than 32°C. Ventricular pacing wires were applied so that cardiac pacing was performed for temporary heart block or bradycardia.

When myocardial function was satisfactory and adequate rewarming had taken place the pulmonary artery needles were removed and their insertion sites oversewn. The SVC cannula was withdrawn into the right atrium and the IVC cannula removed. Cardiopulmonary bypass was slowly discontinued. A pulmonary artery catheter was inserted into the jugular vein or superior vena cava and cardiac output measurement made. If the cardiac performance was satisfactory, the aortic and SVC cannulae was removed. Any drugs considered necessary to maintain good cardiac function were administered and documented in the study records. The heparin was reversed with use of [redacted] in the ratio of approximately [redacted] to [redacted] of circulating heparin. This was usually an underestimate and more was added on the basis of ACT measurements.

Closure

Two drains were inserted, one into the pericardial cavity posterior to the heart and other into the anterior mediastinum. The sternotomy was closed using 4 - 5 heavy ethibond sutures. The subcutaneous tissues was closed in two layers using 3/0 vicryl and the skin was then closed with subcuticular absorbable 4/0 PDS.

POST-OPERATIVE MANAGEMENT

Recovery of the animal commenced immediately following the completion of surgery. As soon as the animal recovered from anaesthesia all drains and intra-arterial lines were removed. The animal was placed in a heated and oxygen saturated cage to help the animal to recover more quickly. When considered sufficiently recovered by the attending veterinary officer/surgeon the animal was returned to its pre-surgery cage.

Recipient animals were closely monitored for the first 48 hours post-operation. Following transplant, heat lamps were used to warm the animals until such time their use was no longer required, as determined by the attending veterinarian.

Following transplantation, on removal from the cage each morning animals were first administered the relevant anti-emetics, then the blood samples were taken, followed by the recording of the electrocardiogram and any other procedures considered necessary and finally the drug was administered. Following completion of all the morning's procedures the animals were then placed back into the cage. This procedure was followed wherever possible to minimise the handling of the animals.

Post-operative analgesia was provided by the use of [redacted] which was administered by intramuscular injection at the discretion of the attending veterinary surgeon. Other drugs were prescribed if considered appropriate. Details of individual drug administrations were recorded in the study records.

Animals received a single administration of [redacted] solution) on the day prior to transplant. From Day 1, a single dose was administered daily (or more frequently if considered necessary) at the discretion of the attending veterinarian. Animals received a subcutaneous injection at a dosage of [redacted]

Dependent on the clinical condition of each animal, food and/or fluid supplements were given at the descretion of the attending veterinary surgeon and/or Sponsor's monitoring scientist (or their deputy). Details of any food and/or fluid supplements which were given to animals were recorded in the study daybook.

POST-OPERATIVE OBSERVATIONS

Dated and signed records of all activities relating to the day by day running and maintenance of the study within the animal unit, as well as to the group observations and examinations outlined in this protocol, were recorded in the study daybook. In addition, observations relating to individual animals made throughout the day were recorded.

The following observations were made during the course of the study.

Mortality

The circumstances of any death were recorded in detail and a full *post mortem* examination was performed to try and determine the cause of death. Prior to death, observations listed in this protocol were carried out, if practicable.

Clinical signs

All signs of ill health or reaction to treatment were recorded. Animals were checked regularly throughout the working day from approximately 0830 to 1700 hours (including weekends and public holidays).

Following transplant each animal was removed from its cage at least twice daily (*ie* at the time of drug administration) for an assessment of its general condition and inspection of the wound.

Bodyweight

Bodyweight was recorded weekly during the pre-operative period and daily throughout the post-operative period. The animals were weighed in the morning prior to dosing, or at a similar time during the pre-dosing period.

Food consumption

The quantity of food (standard dry diet) left by individual animals together with an estimate of the quantity spilled was recorded on a daily basis throughout the experimental period. From these data the quantities consumed were calculated.

Water consumption

The quantity of water consumed by individual animals was recorded on a daily basis throughout the experimental period.

Urine output

The quantity of urine voided by individual animals was recorded on a daily basis for 24 hours pre-transplant and for the first 48 - 72 hours post transplant for animal X221m.

POST-OPERATIVE INVESTIGATIONS

Electrocardiography

Electrocardiograms (ECGs) were performed on a daily basis post-transplant. Recordings were made at approximately the same time each day (*ie* when animal was removed from its cage in the morning for examination/drug administration).

Recordings were made on a multi-channel electrocardiograph and consist of standard limb lead I, II and III and augmented limb leads aVR, aVL, aVF. A standardisation of 10 mm = 1 mV was used and a paper speed of 25 mm/second. An additional recording of lead II was taken at a paper speed of 50 mm/second.

The recordings were examined visually by the Sponsor's Monitoring Scientist to assist in the clinical management of individual animals. This data has not been included in this report.

Blood sampling

Blood samples were taken on Mondays, Wednesdays and Fridays for all animals throughout the post-operative period. Subsequent to 1 April 1996 haematology investigations were performed daily for the first 5 days following transplant and subsequent to 25 July haematology investigations were performed daily for the first 2 weeks following transplant. Blood samples for measurement of anti-pig antibody levels were obtained daily following transplant. Any amendment to the blood sampling schedule was recorded in the study records. Blood samples were taken in the morning prior to any dosing for the following investigations:

Haematology	Units
0.3 ml into 0.5 ml EDTA tube. The following investigations were performed using a Bayer-Technicon H1E haematology analyser	
Packed cell volume (PCV)	%
Haemoglobin (Hb)	g/dl
Red blood cell count (RBC)	$\times 10^{12}$/l
Total white cell count (WBC Total)	$\times 10^{9}$/l
Platelet count (Plts)	$\times 10^{9}$/l

			Units
Differential WBC count			
Neutrophils	(N)	)	
Lymphocytes	(L)	)	
Eosinophils	(E)	)	$\times 10^9/l$
Basophils	(B)	)	
Monocytes	(M)	)	
Large unstained cells	(LUC)	)	

Cell Morphology : the most common morphological changes (anisocytosis, micro/macrocytosis, variation in colour, hypo/hyperchromasia, left shift, atypical/blast cells) were recorded as follows:

- . = No abnormalities detected
- \+ = slight
- ++ = moderate
- +++ = marked

In the case of atypical/blast cells, or other abnormalities, confirmation or a written description from a blood film was made.

Biochemistry

0.7 ml into heparinised microtainer. The following parameters were analysed with a Hitachi 737 Clinical Chemistry analyser

Total protein (Total Prot)	g/dl
Globulin (Glob): by subtraction Total protein (g/dl) minus Albumin (g/dl)	g/dl
Urea	mg/dl
Creatinine (Creat)	mg/dl
Sodium (Na)	mEq/l
Potassium (K)	mEq/l
Calcium (Ca)	mEq/l
Inorganic Phosphorus (P)	mEq/l
Chloride (Cl)	mEq/l

	Units
Osmolality (Osmol) - using a Wescor vapour-pressure osmometer	mOsm/kg
* Total Bilirubin (Bilirubin)	mg/dl
Alkaline phosphatase (AP) Reaction temperature 30°C	mU/ml

The following parameters were analysed using a Roche Cobas Centrifugal analyser, using the appropriate BCL test kit:

* Glutamic pyruvic transaminase (GPT), also known as 'alanine aminotransferase' Reaction temperature 30°C	mU/ml
Glutamic-oxaloacetic transaminase (GOT), also known as 'Aspartate aminotransferase' Reaction temperature 30°C	mU/ml

* These parameters were only investigated for individual animals if indicated by their clinical condition and as recommended by the Sponsor or attending Veterinarian.

(b) Blood samples for despatch to [redacted] or [redacted]

Anti-pig antibody levels (Serum)

0.5 ml into plain microtainer. Samples were analysed at [redacted] for anti-pig antibody levels. Samples were obtained initially on Day -1 and thereafter at the request of the Sponsor.

[redacted]

0.2 ml into 0.5 ml EDTA tube. Samples were analysed at [redacted] for [redacted] level.

Where samples were stored prior to despatch, they were spun, separated and stored deep frozen.

TERMINAL STUDIES

The animals were maintained and dosed according to the immunosuppressive protocol unless sacrifice was required due to one of the following events occurring.

1. Evidence of heart failure. Signs of xenograft rejection were manifest by the absence of papable or audible cardiac activity or the absence of ECG activity.

2. Breakdown or marked infection of any wound site.

3. Systemic illness or marked deviation from its usual state of health.

4. Upon the advice of veterinary surgeons.

The Sponsor was contacted before any decision was taken to sacrifice an animal.

Pre-terminal blood sampling

Prior to sacrifice as much blood as practicable was collected and divided appropriately into heparinised and plain blood tubes.

Following centrifugation the plasma and serum was separated and deep frozen (in cardice) prior to despatch to the Sponsor for analysis.

Necropsy procedure

After the xenograft had been handled, all surfaces were cleaned and gloves were changed to minimise the possibility of contamination.

Each animal was immobilised with [redacted] given by the intramuscular route. The animals were then killed by a lethal dose of [redacted] and then rapidly exsanguinated by incision of the carotid blood vessels.

Immediately after exsanguination the xenograft with its associated anastomoses was carefully removed and weighed. A small section from the wall of each of the four chambers was taken and placed on a cork disc, covered in OCT-embedding matrix ([redacted]) and rapidly frozen in liquid nitrogen. Each section was then individually wrapped in foil and stored deep frozen (in cardice) prior to despatch to the Sponsor. Four sections of the left ventrical were retained for Electron Microscopy.

The remainder of the heart, with the exception of samples for virus studies (see overleaf), was placed in neutral-buffered formalin.

Additional tissue samples of spleen were taken from all animals at *post mortem* as follows:

- two pieces of spleen were collected into cryovials and frozen in liquid nitrogen
- two pieces of spleen were placed on cork discs, covered in OCT-embedding matrix and rapidly frozen in liquid nitrogen. Each piece was then wrapped in foil.

Frozen samples were stored in cardice. All samples were despatched to the Sponsor together with the other protocol-listed tissues.

PROCEDURES

The procedures used during the study were documented in the relevant Huntingdon Life Sciences Procedures Manuals with the exception of the surgical procedures for which there were no SOPs available.

DEVIATIONS FROM PROTOCOL

There were no deviations from protocol other than those documented in the study records and which related to the clinical management of individual animals on a day-to-day basis.

Virus studies

Samples of the following tissues were required fromall recipient animals where the cardiac xenograft had survived in excess of 5 days. The size of the sample was ideally approximately 0.5 cm^3 or if this size was not possible, as much as was feasible.

- transplanted heart
- vascular anastomoses
- kidney
- lung
- liver
- testes
- pancreas
- brain
- ileum
- mid-colon
- sternum
- spleen
- regional draining lymph nodes
- plasma

All samples were taken in triplicate. For individual animals other tissue samples were taken at the discretion of the Sponsor's Monitoring Scientist.

All samples were snap frozen in liquid nitrogen and stored deep frozen (*ca* -70°C) prior to despatch to the Sponsor.

LOCATION OF STUDY RECORDS

All specimens (except those sent to the Sponsor or other third party), raw data and other documents generated at Huntingdon Life Sciences, together with a copy of the final report were lodged in the Huntingdon Life Sciences, Archives, Huntingdon, England.

Such specimens and records were retained for a minimum period of five years from the date of issue of this final report. At the end of the five year retention period the Client will be contacted and advice sought on their future requirements. Under no circumstances will any item be discarded without the Client's knowledge.

The Sponsor was responsible for the retention and archiving of those tissue and plasma/serum samples despatched to them during the course of the study. Data arising from any investigations made by the Sponsor or other third party, the findings of which are included in the Huntingdon Life Sciences final report, was retained and archived by the Sponsor

APPENDIX 10

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day, the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1) except where the animal did not survive beyond Day 0.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day No.		Observation
W213m	1	am	Quiet but alert, becomes active when stimulated.
		pm	Quiet but alert, becomes active when stimulated.
	2	am	Quiet and still but alert and upright.
		pm	Quiet but alert, some occasional activity.
	3	am	Quiet but reasonably alert, huddled.
		pm	Quiet but reasonably alert, huddled. Observed vomiting.
	4	am	Quiet but alert, unusual posture, loose faeces.
		pm	Quiet but alert.
	5	am	Quiet but alert, swelling on lower abdomen, no faeces seen.
		pm	Quiet but alert, no faeces seen.
	6	am	Quiet but alert, swelling on lower abdomen , normal faeces.
		pm	Quiet but alert, occasionally huddled, occasionally sits or lays on cage floor.
	7	am	Quiet but alert, huddled, swelling around wound and lower abdomen.
		pm	Quiet but alert, huddled, swelling around wound and lower abdomen , liquid faeces contained some blood stained mucus, observed shivering.
	8	am	Quiet but alert, huddled, occasionally collapsed on cage floor, liquid faeces, vomit in tray.
		pm	Quiet but alert, dose sites bruised but not bleeding, dark liquid faeces passed.
	9	am	Quiet but alert, body tremors, unsteady movement, dark brown liquid faeces, general bruising around body.
		pm	Sacrificed for humane reasons.
W209m	0	pm	Did not recover from anaesthesia. Cardiac and respiratory arrest at 01.20.
V687m	1	am	Quiet but alert.
		pm	Quiet and huddled, appeared very tired, urine and faeces passed.
	2	am	Quiet but alert, huddled.
		pm	Quiet but alert, huddled, normal faeces.
	3	am	Quiet but alert, huddled, loose/liquid faeces.
		pm	Quiet but alert, huddled , liquid faeces.
	4	am	Quiet but alert, loose/liquid faeces.
		pm	Quiet but alert, loose/liquid faeces.
	5	am	Quiet, slow movements, improved faecal output.
		pm	Weak, difficulty in breathing. Sacrificed for humane reasons.
W203m	0	pm	Did not recover from anaesthesia. Sacrificed for humane reasons.
W211m	1	am	Quiet but alert, huddled, vomited overnight.
		pm	Quiet and huddled, semi-digested food vomit.
	2	am	Quiet but alert, huddled, slightly brighter than on Day 1.
		pm	Alert and active at times moving around cage and sitting on perch.
	3	am	Quiet but alert, loose faeces, semi-digested food vomit.
		pm	Quiet but alert, loose faeces.
	4	am	Quiet but alert, some normal faeces
		pm	Quiet but alert, loose and normal faeces.
	5	am	Quiet but alert, normal faeces
		pm	Quiet and sitting on bottom of cage. Vomit in cage, abdomen swollen. Found dead.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day No.		Observation
X213m	1	am	Sacrificed for humane reasons.
W233m	0	pm	Died before recovery from anaesthesia.
X215m	1	am	Quiet but alert, sitting on cage floor.
		pm	Quiet but alert, sitting on perch, no faeces seen.
	2	am	Quiet but alert, sitting on perch, normal faeces.
		pm	Quiet but alert,
	3	am	Quiet but alert, seated on perch and moving around freely, loose/liquid faeces.
		pm	Unsteady, weak, rapid and slightly harsh breathing, swollen around eyes, laboured breathing, lower abdominal region swollen. Occasionally adopts a sitting position, minimal activity.
	4	am	Quiet and huddled, liquid faeces
		pm	Quiet and huddled, laboured breathing, no response to stimuli, sitting on cage floor, swelling around eyes, oedema on lower abdomen, liquid faeces. Sacrificed for humane reasons.
X219m	0	pm	Sacrificed for humane reasons.
X221m	1	am	Quiet but alert, no faeces seen.
		pm	Quiet but alert, no faeces seen.
	2	am	Quiet but alert, some blood on back shelf, normal faeces.
		pm	Quiet, huddled at back of cage. More alert later (21.00).
	3	am	Quiet, sitting on floor but active when observed.
		pm	Quiet but alert, sitting on floor but active when observed.
	4	am	Quiet but alert, active at times, loose faeces.
		pm	Quiet but alert, no faeces seen.
	5	am	Quiet but alert, vomit on back shelf, loose/liquid faeces. Animal died during examination.

APPENDIX 10

Individual clinical signs

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day, the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1) except where the animal did not survive beyond Day 0.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X239m	1	am	Quiet, appears asleep, sitting on cage floor, occasionally moves around cage, alert/aware if stimulated, breathing appears normal.
		pm	Very subdued, heavy lidded, weak when moving, breathing rate appears to have increased, on return to cage after treatments, breathing heavily and audibly, initially no reaction to external stimuli, after approximately 15 minutes, became more aware of surroundings, breathing more settled.
	2	am	Vomiting. Very quiet but alert when disturbed, urine and faeces passed, appears swollen around the throat. Sacrificed for humane reasons.
X202f	1	am	Quiet but alert, sitting on perch, occasionally asleep.
		pm	Quiet but alert, no faeces or urine passed.
	2	am	Vomited overnight. Quiet but alert, not very active.
		pm	Quiet but alert, sitting on perch at front of cage, breathing appears normal.
	3	am	Quiet but alert. Liquid/loose faeces.
		pm	Sitting on perch. Loose faeces.
	4	am	Quiet and huddled at back of cage, alert if stimulated. Liquid faeces.
		pm	Alert, sitting on perch. Liquid/loose faeces.
	5	am	Quiet but alert and occasionally active. Fluid build-up around abdomen.
		pm	Quiet but alert, sitting on perch or cage floor. Loose faeces.
	6	am	Quiet but alert and occasionally active. Loose dark faeces.
		pm	Quiet but alert, occasionally active. Loose dark faeces.
	7	am	Quiet but alert, sitting huddled in corner of cage, occasionally active
		pm	Quiet but alert, sitting on cage floor after being sedated for thorax xray and having chest drained. Breathing appears normal, abdomen slightly swollen. Loose faeces.
	8	am	Quiet but alert, sitting huddled on floor in corner of cage. Dark faeces.
		pm	Quiet and huddled, eyes partially closed, periodic severe tremors in upper torso and head, later animal appears more comfortable.
	9	am	Quiet, huddled on cage floor, breathing appears shallow but regular. Little resistance to handling.
		pm	Quiet but alert, reluctant to move, breathing appears normal. Loose faeces. Wound slightly open between nipples, cloudy yellow/white discharge seeping from wound.
	10	am	Quiet but alert, eyes closed. Loose faeces.
		pm	Loose faeces.
	11	am	Quiet but alert, split in middle of wound, animal unsteady. Loose faeces. Animal sacrificed for humane reasons.
X210f	0		Died during surgery.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X206f	1	am	Quiet but alert. Urine passed.
		pm	Occasionally active. Loose faeces.
	2	am	Quiet but alert. Chest wound weeping slightly. Loose faeces.
		pm	Quiet but alert. Dark loose faeces.
	3	am	Quiet but alert, breathing appears regular and even. Dark faeces.
		pm	Quiet but alert, occasionally huddled.
	4	am	Quiet but alert, breathing regular. Vomit in tray.
		pm	Quiet but alert, sits upright on shelf.
	5	am	Quiet but alert, breathing regular.
		pm	Quiet but alert, breathing regular.
	6	am	Quiet but alert, breathing regular. Normal faeces.
		pm	Quiet but alert.
	7	am	Quiet, alert when approached or stimulated. Dark faeces.
		pm	Quiet but alert.
	8	am	Quiet, alert when approached or stimulated. Dark faeces.
		pm	Quiet, alert when stimulated. Dark faeces.
	9	am	Subdued, becomes alert and active when approached/stimulated. Dark faeces.
		pm	Quiet, alert when approached/stimulated. Dark faeces.
	10	am	Quiet but alert. Dark faeces.
		pm	Quiet but alert.
	11	am	Quiet but alert. Dark faeces.
		pm	Quiet but alert and occasionally active. Normal faeces.
	12	am	Quiet but alert.
		pm	Alert, gentle activity.
	13	am	Quiet but alert and vocalising, occasionally active. Dark faeces.
		pm	Quiet but alert and vocalising, reasonably active. Dark faeces.
	14	am	Pre-dose - bright and alert, reacts to stimuli. After dose - Huddled and subdued. Dark faeces.
		pm	Asleep in corner of cage, normal faeces.
	15	am	Alert and slightly active. Dark faeces.
		pm	Quiet and huddled, alert when stimulated. Dark faeces.
	16	am	Alert and active when stimulated. Normal faeces.
		pm	Quiet but alert and occasionally active. Dark faeces.
	17	am	Quiet but alert and occasionally active. Dark faeces.
		pm	Quiet but alert and occasionally active. Dark faeces.
	18	am	Quiet, alert, slightly active, sitting on shelf. Dark faeces.
		pm	Alert, sitting on perch. Normal faeces.
	19	am	Quiet, alert slightly active, sitting on perch. Dark faeces.
		pm	Quiet but alert and occasionally active. Normal faeces.
	20	am	Quiet but alert, sitting on perch. Dark faeces.
		pm	Alert and fairly active. Normal faeces.
	21	am	Quiet but alert, sitting on shelf. Dark faeces.
		pm	Quiet but alert, sitting on perch. Approximately 10 mls brown vomit. Dark faeces.
	21/22	o/n	Continuously lying down, noisy laboured respiration, extreme difficulty breathing, vocalising. Died prior to sacrifice (01.17 am).

o/n Overnight observation

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X234f	1	am	Comment not recorded
		pm	Alert, sitting on perch, slow movements.
	2	am	Alert, sitting upright at front of cage, moves when stimulated. Normal faeces.
		pm	Breathing appears regular. Observed vomiting.
	3	am	Quiet, sitting at back of cage, alert when stimulated. Dark loose faeces.
		pm	Quiet, sitting at front of cage, alert when stimulated. Dark loose faeces.
	4	am	Quiet but alert, some activity moving around cage. No faeces.
		pm	Quiet but alert, occasionally becoming active. No faeces.
	5	am	Quiet but alert, occasionally active. Dark faeces.
		pm	Quiet but alert, sitting at front of cage. No faeces.
	6	am	Quiet but alert, occasionally active. Dark faeces.
		pm	Quiet but alert, sitting on perch, fairly active. Normal faeces.
	7	am	Alert, sitting on perch, resting on stomach. Dark faeces.
		pm	Quiet but alert, sitting on cage floor. No faeces.
	8	am	Alert, sitting on perch. Dark faeces.
		pm	Quiet but alert, moving around cage. Dark faeces.
	9	am	Alert, sitting on perch, occasionally active. Dark faeces.
		pm	Alert, occasionally active. Normal faeces.
	10	am	Clear fluid seeping from wound when being handled.
		pm	Quiet but alert. No faeces.
	11	am	Quiet but alert, sitting on perch, fairly active. Normal faeces.
		pm	Quiet but alert, reasonably active.
	12	am	Quiet but alert, occasionally active. Dark faeces.
		pm	Animal quiet and deteriorating rapidly. Sacrificed for humane reasons.
X201m	1	am	Alert, aware of surroundings, slightly unsteady, urine passed.
		pm	Slow moving but aware of surroundings. Dark loose faeces.
	2	am	Sitting on perch, constantly resting head, very slow movements. Loose faeces.
		pm	Quiet but alert, sitting on perch.
	3	am	Alert and fairly active. Loose faeces.
		pm	Alert and active. Normal faeces.
	4	am	Alert and fairly active, sitting on cage floor, vocalising.
		pm	Quiet and huddled but alert and responds quickly to external stimuli.
	5	am	Alert and fairly active. Dark faeces.
		pm	Alert and occasionally active. Dark faeces.
	6	am	Alert and fairly active. Dark faeces.
		pm	Quiet but alert, sitting on perch. Dark faeces
	7	am	Alert and active. Normal faeces.
		pm	Alert and active. Normal faeces.
	8	am	Alert and fairly active. Dark faeces.
		pm	Alert and fairly active. Dark faeces.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X201m (cont)	9	am	Quiet but alert, occasionally active. Dark faeces.
		pm	Quiet but alert, moving around cage. Dark faeces.
	10	am	Quiet but alert, occasionally active and vocalising. Dark faeces.
		pm	Sitting on sawdust.
	11	am	Alert, gentle activity, vocalising. Normal faeces.
		pm	Quiet but alert, sitting on perch, slightly active.
	12	am	Quiet but alert, sitting on shelf, some activity and vocalisation. Dark faeces.
		pm	Alert and active. Normal faeces.
	13	am	Alert and occasionally active, vocalising.
		pm	Quiet, sitting in cage corner on shelf, appears to be trying to sleep.
	14	am	Alert and occasionally active, vocalising.
		pm	Quiet but alert, occasionally active.
	15	am	Quiet and huddled, reluctant to move, some abdominal breathing seen, slightly unsteady.
		pm	Quiet but alert, sitting on wooden base.
	16	am	Quiet and huddled, reluctant to move.
		pm	Alert and fairly active.
	17	am	Alert and active.
		pm	Alert and active, Dark/orange urine.
	18	am	No comment recorded.
		pm	Alert and active.
	19	am	Alert and active, occasionally huddled.
		pm	Alert and active. Dark faeces.
	20	am	Alert and active. Normal faeces.
		pm	Quiet but alert at times.
	21	am	Alert, not very active, sitting on perch.
		pm	Quiet and huddled, alert if stimulated. Slow movements, slight abdominal breathing.
	22	am	Alert, not very active, sitting on perch.
		pm	Quiet but alert, sitting on perch.
	23	am	Quiet and fairly active. Dark faeces.
		pm	Quiet but alert, occasionally active.
	24	am	Alert and active, breathing appears normal, small hole in wound. Dark faeces.
		pm	Alert and fairly active.
	25	am	Alert and active. Dark faeces.
		pm	Recovering from sedation.
	26	am	Alert and fairly active, sitting on perch
		pm	Quiet, sitting on perch, reluctant to move/some movement.
	27	am	Quiet but alert, sitting on perch, fairly active. Dark faeces.
		pm	Alert and active, vomiting. Wound appears okay.
	28	am	Alert, occasional activity. Dark faeces.
		pm	Alert, occasional activity.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X201m (cont)	29	am	Quiet but alert, huddled on perch, responds to external stimuli, reluctant to move. Dark faeces.
		pm	Quiet and huddled on perch, appears asleep. Normal faeces.
	30	am	Quiet and huddled but alert if stimulated, sitting on perch, occasionally active.
		pm	Alert but not active, sitting on perch
	31	am	Huddled but alert, reluctant to move when stimulated.
		pm	No comment recorded.
	32	am	Alert, active, occasional vocalisation. Dark faeces.
		pm	Quiet but alert, occasional activity.
	33	am	Quiet but alert, occasionally active, sitting on wooden base. Dark faeces.
		pm	Quiet but alert, occasional activity. Dark faeces.
	34	am	Quiet but alert, sitting on perch, aggressive and active when stimulated. Dark faeces.
		pm	Quiet but alert, unresponsive to stimulation, sitting on cage floor. Normal faeces.
	35	am	Sitting on perch, huddled but not asleep.
		pm	Quiet and huddled on perch.
	36	am	Sitting on perch, huddled but not asleep, alert when approached.
		pm	Biopsy performed under anaesthetic.
	37	am	Huddled, sitting on ledge, reluctant to move.
		pm	Quiet and huddled, alert when stimulated. Dark faeces.
	38	am	Alert but no movement, moves when stimulated. Normal faeces.
		pm	Quiet but alert when approached.
	39	am	Asleep in corner of cage, reluctant to move when stimulated. Dark faeces.
		pm	Very subdued, reluctant to move even when stimulated. Died following collapse.

EXPERIMENTAL PROCEDURE

ANIMAL SUPPLY

A total of 12 (9 male and 3 female) captive-bred cynomolgus monkeys (*Macaca fascicularis*) were allocated to the study from stock held at Huntingdon. The animals were bred at [redacted] and were imported through a UK commercial supplier [redacted]. The age of the animals at allocation to the study was 2 - 3 years and their weights were in the range 2.1 to 3.3 kg.

ANIMAL MANAGEMENT

Cynomolgus monkeys

All animals were conditioned in England for at least 4 weeks before delivery to Huntingdon Life Sciences. Documentation received from the supplier included details relating to quarantine dates, health screening and any treatment administered during the conditioning period. On arrival at Huntingdon Life Sciences they were examined by a Veterinary Officer and allocated a unique colony number, which was tattooed under the right arm. Intrapalpebral tuberculin tests were performed at intervals of approximately 6 weeks, beginning soon after arrival. For transplanted animals, due to the frequency of planned laboratory investigations and due to the nature of the study, intrapalpebral tuberculin testing was stopped following transplant.

The animals were housed in groups of three in cages specifically designed to house non-human primates in clean and secure conditions. The animals were housed in cages measuring 78 cm wide, 103 cm deep and 230 cm high. The cages were constructed of a stainless steel framework and printboard' walls, shelves and ceiling, incorporating a squeeze-back system, food hopper, water bottle holder and a removable 2.5 × 2.5 cm grid floor. Under the front half of each cage was a removable tray which contained wood chippings (Gold Chips sawdust [redacted] for use as a litter/forage substrate. The cages were cleaned and litter replaced each day after recording any food residues. Automatic drinking valves, for the supply of drinking water, were used and were fitted in both upper and lower parts of the cage and were tested each day.

The room in which the animals were kept was as far as practicable isolated from external disturbances. The room temperature was maintained in the range 18 to 22°C, using heat exchangers connected to hot water supplied from oil-fuelled boilers. Relative humidity was maintained in the range 36 to 80%. The environment was governed by a computer controlled building management system which continuously monitored the temperature and humidity controls and the operational state of the air handling plant. Temperature and relative humidity were recorded using a Rototherm Recorder. Deviations in temperature and/or relative humidity outside the set limits (20 - 26°C, 45 - 70%RH) were generally due to the use of fan heaters as supplementary heat sources and when water was used to wash down cages and/or floor. Artificial lighting was used and was controlled to give 12 hours of light and 12 hours of dark per 24 hours. Air extraction was via a balanced system designed to give fifteen air changes per hour.

FOOD AND WATER

Cynomolgus monkeys were each offered 150 grams, of standard dry diet (Primate Diet [redacted], daily. [Subgroup 1 were incorrectly offered 200 g of diet on Day 0]. The following morning, the residue of the previous day was removed and weighed. All animals were starved overnight prior to operation.

Water was available at all times. Vitamin C (Blackcurrant, [redacted]) and [redacted] (a vitamin B_{12} preparation, [redacted]) were added to the drinking water on one day of each week.

There was no information available to the Study Director to indicate that any non-nutrient substance likely to influence the effect of the test substance could reasonably be expected to be present in the diet or the drinking water, both of which are routinely subjected to chemical analysis. Results of all the analyses were lodged in the HRC Archives.

Wholemeal bread and fresh fruit or vegetable produce was sometimes offered in order to enrich the environment and improve the interaction between the animals and their handlers.

STUDY DESIGN

The monkeys allocated to the study received grafts of meniscal cartilage from either transgenic (hDAF +ve) or control (hDAF -ve) pigs. A total of 12 animals (9 males and 3 females) therefore received either transgenic or control xenografts.

For blinding purposes, the meniscal cartilage used for each transplant was identified by number only and randomly allocated for grafting. The allocation of individual animals to each group (hDAF +ve) or (hDAF -ve) could therefore not be specified.

Transplants were performed on 6 animals per day and were performed on two days a week apart. The commencement of the study for each sub-group, therefore, varied depending on which date the transplant was performed.

Animals were identified by their colony number. The identities of the animals allocated to the study were as follows:

Sub-group	Animal nos.
1	X35m, X37m, X43m, X45m, X47m, X49m
2	V783m, W29m, W761m, W[illegible]f, W466f, X32f

The animals were housed in the [redacted]

PRE-OPERATIVE INVESTIGATIONS

Either on the day of transplant, prior to surgery or on the day before surgery, blood samples were obtained from animals for the following investigations:

1. Anti-pig antibody titres and mixed lymphocyte reaction
2. Anti-collagen and anti-proteoglycan antibody titres
3. Routine haematological and biochemical investigations

See POST-OPERATIVE INVESTIGATIONS for the type of sample and investigations to be performed.

SURGICAL PROCEDURE (including anaesthetic management)

The day of transplant was designated Day 0.

All animals were starved overnight prior to surgery. Prior to transfer to the operating theatre the animal was sedated with [redacted] given by the intramuscular route in combination with [redacted]).

Following induction of anaesthesia by intravenous injection of [redacted] an endotracheal tube was inserted and the animals were maintained on a [redacted] with the addition of [redacted] at a concentration of [redacted] as required.

Prophylactic antibiotic therapy [redacted], was given by subcutaneous injection on Day 0 and for 3 further days afterwards.

An indwelling cannula was inserted into a peripheral vein for administration of fluids and drugs during the procedure. The animal was transferred to the operating table where appropriate respiratory and electrocardiographic monitoring was established.

One knee and adjacent thigh and leg were shaved. A latex tourniquet was applied to the thigh for the first two animals transplanted (X35, X37), after which it was not considered necessary.

A midline incision was made longitudinally down the front of the knee and into the joint so that the patella could be reflected laterally in the normal way. The medial meniscus was excised. A porcine meniscus was sutured into place using 4/0 undyed vicryl sutures through the coronal ligament. Haemostasis was achieved with diathermy, and the wound was closed with 3/0 undyed vicryl sutures to the capsule and skin. Subcuticular sutures were used to close the skin.

A pressure dressing was applied for 24 hours, or until it was removed by the animal, whichever was sooner.

POST-OPERATIVE MANAGEMENT

Recipient animals were closely monitored until fully recovered from the operation.

Post-operative analgesia was provided by the use of [redacted] which was administered at the discretion of the attending veterinary surgeon. Other drugs, including extension of the antibiotic treatment, were prescribed if considered appropriate. Details of individual drug administrations were recorded in the study records.

Dependent on the clinical condition of each animal, food and/or fluid supplements were given at the discretion of the attending veterinary surgeon and/or Sponsor's monitoring scientist (or their deputy). Details of any food and/or fluid supplements which were given to animals were recorded in the study records.

POST-OPERATIVE OBSERVATIONS

Dated and signed records of all activities relating to the day by day running and maintenance of the study within the animal unit, as well as to the group observations and examinations outlined in this protocol, were recorded in the Study Day Book. In addition, observations relating to individual animals made throughout the day were recorded.

The following observations were made during the course of the study:

Clinical signs

All signs of ill health or reaction to treatment were recorded. Animals were checked regularly throughout the working day from approximately 0800 to 1700 hours (including weekends and public holidays). The animals were removed from their cages at least once a day to examine the condition of the wound and apply any treatments if necessary.

Bodyweight

The bodyweight of all animals was recorded each week throughout the duration of the study.

Food consumption

The quantity of food (standard dry diet) left by each trio of animals together with an estimate of the quantity spilled was recorded on a daily basis throughout the experimental period. From these data the quantities consumed were calculated.

POST-OPERATIVE INVESTIGATIONS

Blood sampling

Blood samples were obtained on Mondays, Wednesdays and Fridays throughout the post-operative period. Blood samples were taken in the morning for the following investigations:

(a) **Laboratory investigations performed at HRC**

Haematology and biochemistry investigations, as detailed below, were performed on one day each week (Wednesday).

Haematology	**Units**
300 µl into 0.5 ml EDTA tube. The following investigations were performed using a Bayer-Technicon H1E haematology analyser:	
Packed cell volume (PCV)	%
Haemoglobin (Hb)	g/dl
Red blood cell count (RBC)	$\times 10^{12}/l$
Total white cell count (WBC Total)	$\times 10^{9}/l$
Platelet count (Plts)	$\times 10^{9}/l$
Differential WBC count (Diff)	
Neutrophils (N) Lymphocytes (L) Eosinophils (E) Basophils (B) Monocytes (M) Large unstained cells (LUC)	$\times 10^{9}/l$

Cell Morphology : the most common morphological changes (anisocytosis, micro/macrocytosis, variation in colour, hypo/hyperchromasia, left shift, atypical/blast cells) were recorded as follows:

- \- = No abnormalities detected
- \+ = slight
- \++ = moderate
- \+++ = marked

In the case of atypical/blast cells, or other abnormalities, confirmation or a written description from a blood film was made.

Biochemistry	Units
700 µl into heparinised microtainer. The following parameters were analysed with a Hitachi 737 Clinical Chemistry analyser:	
Creatinine	mg/dl
Sodium (Na)	mEq/l
Potassium (K)	mEq/l
Calcium (Ca)	mEq/l
Inorganic Phosphorus (P)	mEq/l
Chloride (Cl)	mEq/l

(b) **Blood samples for despatch to [redacted] or [redacted]**

Anti-pig antibody levels (Serum)

0.5 ml into plain tube. Samples were analysed at [redacted] for anti-pig antibody levels.

Anti-collagen and anti-proteoglycan antibody titres

0.5 ml into plain tube.

Mixed lymphocyte reaction

1ml into heparin.

The blood samples were obtained in the morning. Samples for [redacted] were despatched so as to arrive no later than 11.00 am.

TERMINAL STUDIES

The animals were maintained nominally for 30 or 60 days following transplant after which they were sacrificed. Due to the availability of the Sponsor's surgeon terminal procedures were actually performed on Days 30 and 62 for Subgroup 1 and Days 33 and 57 for Subgroup 2.

Pre-terminal blood sampling

Prior to sacrifice as much blood as practicable was collected and divided appropriately into heparinised and plain blood tubes.

Following centrifugation the plasma/serum was separated and stored deep frozen (in cardice) prior to despatch to the Sponsor for analysis.

Necropsy procedure

Each animal was immobilised with [redacted] given by the intramuscular route. The animals were then killed by a lethal dose of [redacted] and then rapidly exsanguinated by incision of the carotid blood vessels.

Immediately after exsanguination both knee joints were dissected free of soft tissue and removed. The knee joints were frozen in liquid nitrogen and stored deep frozen in cardice prior to despatch to the Sponsor for examination.

Virus studies

Samples of the following tissues were taken from all recipient animals. The size of the sample was ideally approximately 0.5 cm^3 or if this size was not possible, as much as feasible.

- kidney
- heart
- lung
- liver
- ovaries or testes
- spleen
- pancreas
- brain
- ileum
- mid-colon
- sternum
- mesenteric lymph node
- retro-peritoneal lymph node
- inguinal lymph node

All samples were snap frozen in liquid nitrogen and stored deep frozen (*ca* -70°C).

LOCATION OF STUDY RECORDS

All raw data, samples and specimens arising from the performance of this study will remain the property of the Sponsor.

All specimens sent to the Sponsor or other Sponsor-nominated laboratory are the responsibility of the Sponsor in respect of storage and archiving. Data and other records arising from any investigations performed on these specimens will be retained and archived by the Sponsor.

All other samples and specimens and all other raw data will be retained by Huntingdon Life Sciences in its archive for a period of five years from the date on which the Study Director signs the final report. After such time, the Sponsor will be contacted and his advice sought on the return, disposal or further retention of the materials. If requested, Huntingdon Life Sciences will continue to retain the materials subject to a reasonable fee being agree with the Sponsor.

Huntingdon Life Sciences will retain the Quality Assurance records relevant to this study and a copy of the final report in its archive indefinately.

PROCEDURES

The procedures used during the study, with the exception of the anaesthesia and surgical procedures, were documented in the relevant Huntingdon Life Sciences Procedures Manuals.

DEVIATIONS FROM PROTOCOL

Deviations from protocol have been detailed in an appropriate File Note retained with the relevant study records.

There were no deviations considered to have significantly impacted on the integrity or the outcome of the study.

APPENDIX 6

Explanatory notes

1. Only first (am) and last (pm) observations of the day are reported. Due to manipulations/investigations performed on animals during the day the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1).

Abbreviations

am	Morning
pm	Afternoon

APPENDIX 6

Clinical signs

Animal no./sex	Day no.	Clinical signs
X35m	1 am	Not using right leg.
	pm	Limited use of right leg.
	2 am	Some use of right leg.
	pm	Some use of right leg.
	3 am	Some use of right leg.
	pm	Some use of right leg.
	4 am	Some use of right leg.
	pm	Some use of right leg.
	5 am	Some use of right leg.
	pm	Some use of right leg.
	6 am	Some use of right leg.
	pm	Some use of right leg.
	7 am	Some use of right leg.
	pm	Some use of right leg.
	8 am	Some use of right leg.
	pm	Some use of right leg.
	9 am	Some use of right leg.
	pm	Some use of right leg.
	10 am	Some use of right leg.
	pm	Some use of right leg.
	11 am	Some use of right leg.
	pm	Some use of right leg.
	12 am	Some use of right leg.
	pm	Some use of right leg.
	13 am	Some use of right leg.
	pm	Some use of right leg.
	14 am	Some use of right leg.
	pm	Some use of right leg.
	15 am	Some use of right leg.
	pm	Some use of right leg.
	16 am	Some use of right leg.
	pm	Some use of right leg.
	17 am	Some use of right leg.
	pm	Some use of right leg.
	18 am	Some use of right leg.
	pm	Some use of right leg.
	19 am	Some use of right leg.
	pm	Some use of right leg.
	20 am	Some use of right leg.
	pm	Some use of right leg.
	21 am	Some use of right leg.
	pm	Some use of right leg.
	22 am	Some use of right leg.
	pm	Some use of right leg.
	23 am	Some use of right leg.
	pm	Some use of right leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
X35m (contd)	24 am	Swollen right knee.
	pm	Swollen right knee.
	25 am	Swollen right knee.
	pm	Swollen right knee.
	26 am	Swollen right knee.
	pm	Swollen right knee.
	27 am	Swollen right knee.
	pm	Swollen right knee.
	28 am	Some use of right leg.
	pm	Some use of right leg.
	29 am	Some use of right leg.
	pm	Some use of right leg.
	30 am	Some use of right leg.
	pm	Sacrificed
X37m	1 am	Not using left leg.
	pm	Not using left leg.
	2 am	Some use of left leg.
	pm	Some use of left leg.
	3 am	Quiet and huddled.
	pm	Quiet and huddled.
	4 am	Some use of left leg.
	pm	Some use of left leg.
	5 am	Some use of left leg.
	pm	Some use of left leg.
	6 am	Some use of left leg.
	pm	Some use of left leg.
	7 am	Some use of left leg.
	pm	Some use of left leg.
	8 am	Some use of left leg.
	pm	Some use of left leg.
	9 am	Some use of left leg.
	pm	Some use of left leg.
	10 am	Some use of left leg.
	pm	Some use of left leg.
	11 am	Some use of left leg.
	pm	Some use of left leg.
	12 am	Some use of left leg.
	pm	Some use of left leg.
	13 am	Some use of left leg.
	pm	Some use of left leg.
	14 am	Some use of left leg.
	pm	Some use of left leg.
	15 am	Some use of left leg.
	pm	Some use of left leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
X37m (contd)	16 am	Some use of left leg.
	pm	Some use of left leg.
	17 am	Some use of left leg.
	pm	Some use of left leg.
	18 am	Some use of left leg.
	pm	Some use of left leg.
	19 am	Some use of left leg.
	pm	Some use of left leg.
	20 am	Some use of left leg.
	pm	Some use of left leg.
	21 am	Some use of left leg.
	pm	Some use of left leg.
	22 am	Some use of left leg.
	pm	Some use of left leg.
	23 am	Some use of left leg.
	pm	Some use of left leg.
	24 am	Some use of left leg.
	pm	Some use of left leg.
	25 am	Some use of left leg.
	pm	Some use of left leg.
	26 am	Some use of left leg.
	pm	Some use of left leg.
	27 am	Some use of left leg.
	pm	Some use of left leg.
	28 am	Some use of left leg.
	pm	Some use of left leg.
	29 am	Some use of left leg.
	pm	Some use of left leg.
	30 am	Some use of left leg.
	pm	Some use of left leg.
	31 am	Some use of left leg.
	pm	Some use of left leg.
	32 am	Some use of left leg.
	pm	Some use of left leg.
	33 am	Some use of left leg.
	pm	Some use of left leg.
	34 am	Some use of left leg.
	pm	Some use of left leg.
	35 am	Some use of left leg.
	pm	Some use of left leg.
	36 am	Some use of left leg.
	pm	Some use of left leg.
	37 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	38 am	Some use of left leg.
	pm	Some use of left leg.
	39 am	Some use of left leg.
	pm	Some use of left leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
X37m (contd)	40 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	41 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	42 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	43 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	44 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	45 am	Some use of left leg. Loose/normal faeces.
	pm	Some use of left leg. Normal faeces.
	46 am	Some use of left leg.
	pm	Some use of left leg.
	47 am	Some use of left leg.
	pm	Some use of left leg.
	48 am	Some use of left leg.
	pm	Some use of left leg.
	49 am	Some use of left leg.
	pm	Some use of left leg.
	50 am	Some use of left leg.
	pm	Some use of left leg.
	51 am	Some use of left leg.
	pm	Some use of left leg.
	52 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	53 am	Some use of left leg.
	pm	Some use of left leg.
	54 am	Some use of left leg.
	pm	Some use of left leg.
	55 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	56 am	Some use of left leg.
	pm	Some use of left leg.
	57 am	Some use of left leg.
	pm	Some use of left leg. Loose/normal faeces.
	58 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	59 am	Some use of left leg.
	pm	Some use of left leg.
	60 am	Some use of left leg.
	pm	Some use of left leg.
	61 am	Some use of left leg. Loose/normal faeces.
	pm	Some use of left leg. Loose/normal faeces.
	62 am	Some use of left leg.
	pm	Sacrificed

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
X43m	1 am	Not using right leg.
	pm	Limited use of right leg.
	2 am	Some use of right leg.
	pm	Some use of right leg.
	3 am	Some use of right leg.
	pm	Some use of right leg.
	4 am	Some use of right leg.
	pm	Some use of right leg.
	5 am	Some use of right leg.
	pm	Some use of right leg.
	6 am	Some use of right leg. Some bruising and dry scabs on knee.
	pm	Some use of right leg. Some bruising and dry scabs on knee.
	7 am	Some use of right leg.
	pm	Some use of right leg.
	8 am	Some use of right leg.
	pm	Some use of right leg.
	9 am	Some use of right leg.
	pm	Some use of right leg.
	10 am	Some use of right leg.
	pm	Some use of right leg.
	11 am	Some use of right leg.
	pm	Some use of right leg.
	12 am	Some use of right leg.
	pm	Some use of right leg.
	13 am	Some use of right leg.
	pm	Some use of right leg.
	14 am	Some use of right leg.
	pm	Some use of right leg.
	15 am	Some use of right leg.
	pm	Some use of right leg.
	16 am	Some use of right leg.
	pm	Some use of right leg.
	17 am	Some use of right leg.
	pm	Some use of right leg.
	18 am	Some use of right leg.
	pm	Some use of right leg.
	19 am	Some use of right leg.
	pm	Some use of right leg.
	20 am	Some use of right leg.
	pm	Some use of right leg.
	21 am	Some use of right leg.
	pm	Some use of right leg.
	22 am	Some use of right leg.
	pm	Some use of right leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
X43m (contd)	23 am	Some use of right leg.
	pm	Some use of right leg.
	24 am	Some use of right leg.
	pm	Some use of right leg.
	25 am	Some use of right leg.
	pm	Some use of right leg.
	26 am	Some use of right leg.
	pm	Some use of right leg.
	27 am	Some use of right leg.
	pm	Some use of right leg.
	28 am	Some use of right leg.
	pm	Some use of right leg.
	29 am	Some use of right leg.
	pm	Some use of right leg.
	30 am	Some use of right leg.
	pm	Sacrificed.
X45m	1 am	Not using left leg.
	pm	Limited use of left leg.
	2 am	Some use of left leg.
	pm	Some use of left leg.
	3 am	Quiet and huddled.
	pm	Quiet and huddled.
	4 am	Some use of left leg.
	pm	Some use of left leg.
	5 am	Some use of left leg.
	pm	Some use of left leg.
	6 am	Some use of left leg.
	pm	Some use of left leg.
	7 am	Some use of left leg.
	pm	Some use of left leg.
	8 am	Some use of left leg.
	pm	Some use of left leg.
	9 am	Some use of left leg.
	pm	Some use of left leg.
	10 am	Some use of left leg.
	pm	Some use of left leg.
	11 am	Some use of left leg.
	pm	Some use of left leg.
	12 am	Some use of left leg.
	pm	Some use of left leg.
	13 am	Some use of left leg.
	pm	Some use of left leg.
	14 am	Some use of left leg.
	pm	Some use of left leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
X45m (contd)	15 am	Some use of left leg.
	pm	Some use of left leg.
	16 am	Some use of left leg.
	pm	Some use of left leg.
	17 am	Some use of left leg.
	pm	Some use of left leg.
	18 am	Some use of left leg.
	pm	Some use of left leg.
	19 am	Some use of left leg.
	pm	Some use of left leg.
	20 am	Some use of left leg.
	pm	Some use of left leg.
	21 am	Some use of left leg.
	pm	Some use of left leg.
	22 am	Some use of left leg.
	pm	Some use of left leg.
	23 am	Some use of left leg.
	pm	Some use of left leg.
	24 am	Some use of left leg.
	pm	Some use of left leg.
	25 am	Some use of left leg.
	pm	Some use of left leg.
	26 am	Some use of left leg.
	pm	Some use of left leg.
	27 am	Some use of left leg.
	pm	Some use of left leg.
	28 am	Some use of left leg.
	pm	Some use of left leg.
	29 am	Some use of left leg.
	pm	Some use of left leg.
	30 am	Some use of left leg.
	pm	Sacrificed.
X47m	1 am	Not using right leg.
	pm	Not using right leg.
	2 am	Some use of right leg.
	pm	Some use of right leg.
	3 am	Some use of right leg.
	pm	Some use of right leg.
	4 am	Some use of right leg.
	pm	Some use of right leg.
	5 am	Some use of right leg.
	pm	Some use of right leg.
	6 am	Some use of right leg.
	pm	Some use of right leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
X47m (contd)	7 am	Some use of right leg.
	pm	Some use of right leg.
	8 am	Some use of right leg.
	pm	Some use of right leg.
	9 am	Some use of right leg.
	pm	Some use of right leg.
	10 am	Some use of right leg.
	pm	Some use of right leg.
	11 am	Some use of right leg.
	pm	Some use of right leg.
	12 am	Some use of right leg.
	pm	Some use of right leg.
	13 am	Some use of right leg.
	pm	Some use of right leg.
	14 am	Some use of right leg.
	pm	Some use of right leg.
	15 am	Some use of right leg.
	pm	Some use of right leg.
	16 am	Some use of right leg.
	pm	Some use of right leg.
	17 am	Some use of right leg.
	pm	Some use of right leg.
	18 am	Some use of right leg.
	pm	Some use of right leg.
	19 am	Some use of right leg.
	pm	Some use of right leg.
	20 am	Some use of right leg.
	pm	Some use of right leg.
	21 am	Some use of right leg.
	pm	Some use of right leg.
	22 am	Some use of right leg.
	pm	Some use of right leg.
	23 am	Some use of right leg.
	pm	Some use of right leg.
	24 am	Some use of right leg.
	pm	Some use of right leg.
	25 am	Some use of right leg.
	pm	Some use of right leg.
	26 am	Some use of right leg.
	pm	Some use of right leg.
	27 am	Some use of right leg.
	pm	Some use of right leg.
	28 am	Some use of right leg.
	pm	Some use of right leg.
	29 am	Some use of right leg.
	pm	Some use of right leg.
	30 am	Some use of right leg.
	pm	Some use of right leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
X47m (contd)	31 am	Some use of right leg.
	pm	Some use of right leg.
	32 am	Some use of right leg.
	pm	Some use of right leg.
	33 am	Some use of right leg.
	pm	Some use of right leg.
	34 am	Some use of right leg.
	pm	Some use of right leg.
	35 am	Some use of right leg.
	pm	Some use of right leg.
	36 am	Some use of right leg.
	pm	Some use of right leg.
	37 am	Some use of right leg. Loose faeces.
	pm	Some use of right leg. Loose faeces.
	38 am	Some use of right leg.
	pm	Some use of right leg.
	39 am	Some use of right leg.
	pm	Some use of right leg.
	40 am	Some use of right leg.
	pm	Some use of right leg.
	41 am	Some use of right leg.
	pm	Some use of right leg.
	42 am	Some use of right leg.
	pm	Some use of right leg.
	43 am	Some use of right leg.
	pm	Some use of right leg.
	44 am	Some use of right leg.
	pm	Some use of right leg.
	45 am	Some use of right leg. Loose faeces.
	pm	Some use of right leg. Normal faeces.
	46 am	Some use of right leg.
	pm	Some use of right leg.
	47 am	Some use of right leg.
	pm	Some use of right leg.
	48 am	Some use of right leg.
	pm	Some use of right leg.
	49 am	Some use of right leg.
	pm	Some use of right leg.
	50 am	Some use of right leg.
	pm	Some use of right leg.
	51 am	Some use of right leg.
	pm	Some use of right leg.
	52 am	Some use of right leg. Loose faeces.
	pm	Some use of right leg. Loose faeces.
	53 am	Some use of right leg.
	pm	Some use of right leg.
	54 am	Some use of right leg.
	pm	Some use of right leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
X47m (contd)	55 am	Some use of right leg. Loose faeces.
	pm	Some use of right leg. Loose faeces.
	56 am	Some use of right leg.
	pm	Some use of right leg.
	57 am	Some use of right leg.
	pm	Some use of right leg. Loose faeces.
	58 am	Some use of right leg. Loose faeces.
	pm	Some use of right leg. Loose faeces.
	59 am	Some use of right leg.
	pm	Some use of right leg.
	60 am	Some use of right leg.
	pm	Some use of right leg.
	61 am	Some use of right leg. Loose faeces.
	pm	Some use of right leg. Loose faeces.
	62 am	Some use of right leg.
	pm	Sacrificed.
X49m	1 am	Not using left leg.
	pm	Limited use of left leg.
	2 am	Some use of left leg.
	pm	Some use of left leg.
	3 am	Some use of left leg.
	pm	Some use of left leg.
	4 am	Some use of left leg.
	pm	Some use of left leg.
	5 am	Some use of left leg.
	pm	Some use of left leg.
	6 am	Some use of left leg.
	pm	Some use of left leg.
	7 am	Some use of left leg.
	pm	Some use of left leg.
	8 am	Some use of left leg.
	pm	Some use of left leg.
	9 am	Some use of left leg.
	pm	Some use of left leg.
	10 am	Some use of left leg.
	pm	Some use of left leg.
	11 am	Some use of left leg.
	pm	Some use of left leg.
	12 am	Some use of left leg.
	pm	Some use of left leg.
	13 am	Some use of left leg.
	pm	Some use of left leg.
	14 am	Some use of left leg.
	pm	Some use of left leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
X49m (contd)	15 am	Some use of left leg.
	pm	Some use of left leg.
	16 am	Some use of left leg.
	pm	Some use of left leg.
	17 am	Some use of left leg.
	pm	Some use of left leg.
	18 am	Some use of left leg.
	pm	Some use of left leg.
	19 am	Some use of left leg.
	pm	Some use of left leg.
	20 am	Some use of left leg.
	pm	Some use of left leg.
	21 am	Some use of left leg.
	pm	Some use of left leg.
	22 am	Some use of left leg.
	pm	Some use of left leg.
	23 am	Some use of left leg.
	pm	Some use of left leg.
	24 am	Some use of left leg.
	pm	Some use of left leg.
	25 am	Some use of left leg.
	pm	Some use of left leg.
	26 am	Some use of left leg.
	pm	Some use of left leg.
	27 am	Some use of left leg.
	pm	Some use of left leg.
	28 am	Some use of left leg.
	pm	Some use of left leg.
	29 am	Some use of left leg.
	pm	Some use of left leg.
	30 am	Some use of left leg.
	pm	Some use of left leg.
	31 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	32 am	Some use of left leg.
	pm	Some use of left leg.
	33 am	Some use of left leg.
	pm	Some use of left leg.
	34 am	Some use of left leg.
	pm	Some use of left leg.
	35 am	Some use of left leg.
	pm	Some use of left leg.
	36 am	Some use of left leg.
	pm	Some use of left leg.
	37 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	38 am	Some use of left leg.
	pm	Some use of left leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
X49m (contd)	39 am	Some use of left leg.
	pm	Some use of left leg.
	40 am	Some use of left leg.
	pm	Some use of left leg.
	41 am	Some use of left leg.
	pm	Some use of left leg.
	42 am	Some use of left leg.
	pm	Some use of left leg.
	43 am	Some use of left leg.
	pm	Some use of left leg.
	44 am	Some use of left leg.
	pm	Some use of left leg.
	45 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Normal faeces.
	46 am	Some use of left leg.
	pm	Some use of left leg.
	47 am	Some use of left leg.
	pm	Some use of left leg.
	48 am	Some use of left leg.
	pm	Some use of left leg.
	49 am	Some use of left leg.
	pm	Some use of left leg.
	50 am	Some use of left leg.
	pm	Some use of left leg.
	51 am	Some use of left leg.
	pm	Some use of left leg.
	52 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	53 am	Some use of left leg.
	pm	Some use of left leg.
	54 am	Some use of left leg.
	pm	Some use of left leg.
	55 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	56 am	Some use of left leg.
	pm	Some use of left leg.
	57 am	Some use of left leg.
	pm	Some use of left leg. Loose faeces.
	58 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	59 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	60 am	Some use of left leg. Normal faeces.
	pm	Some use of left leg.
	61 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	62 am	Some use of left leg.
	pm	Sacrificed.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
V783m	1 am	Quiet. Some use of right leg.
	pm	Quiet. Some use of right leg.
	2 am	Limited use of right leg.
	pm	Limited use of right leg.
	3 am	Some use of right leg.
	pm	Some use of right leg.
	4 am	Some use of right leg.
	pm	Some use of right leg.
	5 am	Some use of right leg.
	pm	Some use of right leg.
	6 am	Some use of right leg.
	pm	Some use of right leg.
	7 am	Some use of right leg.
	pm	Some use of right leg.
	8 am	Some use of right leg.
	pm	Some use of right leg.
	9 am	Some use of right leg.
	pm	Some use of right leg.
	10 am	Some use of right leg.
	pm	Some use of right leg.
	11 am	Some use of right leg.
	pm	Some use of right leg.
	12 am	Some use of right leg.
	pm	Some use of right leg.
	13 am	Some use of right leg.
	pm	Some use of right leg.
	14 am	Some use of right leg.
	pm	Some use of right leg.
	15 am	Some use of right leg.
	pm	Some use of right leg.
	16 am	Some use of right leg.
	pm	Some use of right leg.
	17 am	Some use of right leg.
	pm	Some use of right leg.
	18 am	Some use of right leg.
	pm	Some use of right leg.
	19 am	Some use of right leg.
	pm	Some use of right leg.
	20 am	Some use of right leg.
	pm	Some use of right leg.
	21 am	Some use of right leg.
	pm	Some use of right leg.
	22 am	Some use of right leg.
	pm	Some use of right leg.
	23 am	Some use of right leg.
	pm	Some use of right leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
V783m (contd)	24 am	Some use of right leg.
	pm	Some use of right leg.
	25 am	Some use of right leg.
	pm	Some use of right leg.
	26 am	Some use of right leg.
	pm	Some use of right leg.
	27 am	Some use of right leg.
	pm	Some use of right leg.
	28 am	Some use of right leg.
	pm	Some use of right leg.
	29 am	Some use of right leg.
	pm	Some use of right leg.
	30 am	Some use of right leg.
	pm	Some use of right leg.
	31 am	Some use of right leg.
	pm	Some use of right leg.
	32 am	Some use of right leg.
	pm	Some use of right leg.
	33 am	Some use of right leg.
	pm	Some use of right leg.
	34 am	Some use of right leg.
	pm	Some use of right leg.
	35 am	Some use of right leg.
	pm	Some use of right leg.
	36 am	Some use of right leg.
	pm	Some use of right leg.
	37 am	Some use of right leg.
	pm	Some use of right leg.
	38 am	Some use of right leg.
	pm	Some use of right leg.
	39 am	Some use of right leg.
	pm	Some use of right leg.
	40 am	Some use of right leg.
	pm	Some use of right leg.
	41 am	Some use of right leg.
	pm	Some use of right leg.
	42 am	Some use of right leg.
	pm	Some use of right leg.
	43 am	Some use of right leg.
	pm	Some use of right leg.
	44 am	Some use of right leg.
	pm	Some use of right leg.
	45 am	Some use of right leg.
	pm	Some use of right leg.
	46 am	Some use of right leg.
	pm	Some use of right leg.
	47 am	Some use of right leg.
	pm	Some use of right leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
V783m (contd)	48 am	Some use of right leg.
	pm	Some use of right leg.
	49 am	Some use of right leg.
	pm	Some use of right leg.
	50 am	Some use of right leg.
	pm	Some use of right leg.
	51 am	Some use of right leg.
	pm	Some use of right leg.
	52 am	Some use of right leg. Loose faeces.
	pm	Some use of right leg. Loose faeces.
	53 am	Some use of right leg. Loose faeces.
	pm	Some use of right leg. Loose faeces.
	54 am	Some use of right leg.
	pm	Some use of right leg.
	55 am	Some use of right leg.
	pm	Some use of right leg.
	56 am	Some use of right leg.
	pm	Some use of right leg.
	57 am	Some use of right leg.
	pm	Sacrificed.
W29m	1 am	Quiet. Not using left leg.
	pm	Quiet. Not using left leg.
	2 am	Some use of left leg.
	pm	Some use of left leg.
	3 am	Some use of left leg.
	pm	Some use of left leg.
	4 am	Some use of left leg.
	pm	Some use of left leg.
	5 am	Some use of left leg.
	pm	Some use of left leg.
	6 am	Some use of left leg.
	pm	Some use of left leg.
	7 am	Some use of left leg.
	pm	Some use of left leg.
	8 am	Some use of left leg.
	pm	Some use of left leg.
	9 am	Some use of left leg.
	pm	Some use of left leg.
	10 am	Some use of left leg.
	pm	Some use of left leg.
	11 am	Some use of left leg.
	pm	Some use of left leg.
	12 am	Some use of left leg.
	pm	Some use of left leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W29m (contd)	13 am	Some use of left leg.
	pm	Some use of left leg.
	14 am	Some use of left leg.
	pm	Some use of left leg.
	15 am	Some use of left leg.
	pm	Some use of left leg.
	16 am	Swollen left knee.
	pm	Swollen left knee.
	17 am	Swollen left knee.
	pm	Swollen left knee.
	18 am	Swollen left knee.
	pm	Swollen left knee.
	19 am	Swollen left knee.
	pm	Swollen left knee.
	20 am	Some use of left leg.
	pm	Some use of left leg.
	21 am	Some use of left leg.
	pm	Some use of left leg.
	22 am	Some use of left leg.
	pm	Some use of left leg.
	23 am	Some use of left leg.
	pm	Some use of left leg.
	24 am	Some use of left leg.
	pm	Some use of left leg.
	25 am	Some use of left leg.
	pm	Some use of left leg.
	26 am	Some use of left leg.
	pm	Some use of left leg.
	27 am	Some use of left leg.
	pm	Some use of left leg.
	28 am	Some use of left leg.
	pm	Some use of left leg.
	29 am	Some use of left leg.
	pm	Some use of left leg.
	30 am	Some use of left leg.
	pm	Some use of left leg.
	31 am	Some use of left leg.
	pm	Some use of left leg.
	32 am	Some use of left leg.
	pm	Some use of left leg.
	33 am	Some use of left leg.
	pm	Sacrificed.
W761m	1 am	Quiet. Not using right leg.
	pm	Quiet. Not using right leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W761m (contd)	2 am	Some use of right leg.
	pm	Some use of right leg.
	3 am	Some use of right leg.
	pm	Some use of right leg.
	4 am	Some use of right leg.
	pm	Some use of right leg.
	5 am	Some use of right leg.
	pm	Some use of right leg.
	6 am	Some use of right leg.
	pm	Some use of right leg.
	7 am	Some use of right leg.
	pm	Some use of right leg.
	8 am	Some use of right leg.
	pm	Some use of right leg.
	9 am	Some use of right leg.
	pm	Some use of right leg.
	10 am	Some use of right leg.
	pm	Some use of right leg.
	11 am	Some use of right leg.
	pm	Some use of right leg.
	12 am	Some use of right leg.
	pm	Some use of right leg.
	13 am	Some use of right leg.
	pm	Some use of right leg.
	14 am	Some use of right leg.
	pm	Some use of right leg.
	15 am	Some use of right leg.
	pm	Some use of right leg.
	16 am	Some use of right leg.
	pm	Some use of right leg.
	17 am	Some use of right leg.
	pm	Some use of right leg.
	18 am	Some use of right leg.
	pm	Some use of right leg.
	19 am	Some use of right leg.
	pm	Some use of right leg.
	20 am	Some use of right leg.
	pm	Some use of right leg.
	21 am	Some use of right leg.
	pm	Some use of right leg.
	22 am	Some use of right leg.
	pm	Some use of right leg.
	23 am	Some use of right leg.
	pm	Some use of right leg.
	24 am	Some use of right leg.
	pm	Some use of right leg.
	25 am	Some use of right leg.
	pm	Some use of right leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W761m (contd)	26 am	Some use of right leg.
	pm	Some use of right leg.
	27 am	Some use of right leg.
	pm	Some use of right leg.
	28 am	Some use of right leg.
	pm	Some use of right leg.
	29 am	Some use of right leg.
	pm	Some use of right leg.
	30 am	Some use of right leg.
	pm	Some use of right leg.
	31 am	Some use of right leg.
	pm	Some use of right leg.
	32 am	Some use of right leg.
	pm	Some use of right leg.
	33 am	Some use of right leg.
	pm	Some use of right leg.
	34 am	Some use of right leg.
	pm	Some use of right leg.
	35 am	Some use of right leg.
	pm	Some use of right leg.
	36 am	Some use of right leg.
	pm	Some use of right leg.
	37 am	Some use of right leg.
	pm	Some use of right leg.
	38 am	Some use of right leg.
	pm	Some use of right leg.
	39 am	Some use of right leg.
	pm	Some use of right leg.
	40 am	Some use of right leg.
	pm	Some use of right leg.
	41 am	Some use of right leg.
	pm	Some use of right leg.
	42 am	Some use of right leg.
	pm	Some use of right leg.
	43 am	Some use of right leg.
	pm	Some use of right leg.
	44 am	Some use of right leg.
	pm	Some use of right leg.
	45 am	Some use of right leg.
	pm	Some use of right leg.
	46 am	Some use of right leg.
	pm	Some use of right leg.
	47 am	Some use of right leg.
	pm	Some use of right leg.
	48 am	Some use of right leg.
	pm	Some use of right leg.
	49 am	Some use of right leg.
	pm	Some use of right leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W761m (contd)	50 am	Some use of right leg.
	pm	Some use of right leg.
	51 am	Some use of right leg.
	pm	Some use of right leg.
	52 am	Some use of right leg. Loose faeces.
	pm	Some use of right leg. Loose faeces.
	53 am	Some use of right leg. Loose faeces.
	pm	Some use of right leg. Loose faeces.
	54 am	Some use of right leg.
	pm	Some use of right leg.
	55 am	Some use of right leg.
	pm	Some use of right leg.
	56 am	Some use of right leg.
	pm	Some use of right leg.
	57 am	Some use of right leg.
	pm	Sacrificed.
W24f	1 am	Quiet. Some use of left leg.
	pm	Quiet. Some use of left leg.
	2 am	Limited use of left leg.
	pm	Limited use of left leg.
	3 am	Some use of left leg.
	pm	Some use of left leg.
	4 am	Some use of left leg.
	pm	Some use of left leg.
	5 am	Some use of left leg.
	pm	Some use of left leg.
	6 am	Some use of left leg.
	pm	Some use of left leg.
	7 am	Some use of left leg.
	pm	Some use of left leg.
	8 am	Some use of left leg.
	pm	Some use of left leg.
	9 am	Some use of left leg.
	pm	Some use of left leg.
	10 am	Some use of left leg.
	pm	Some use of left leg.
	11 am	Some use of left leg.
	pm	Some use of left leg.
	12 am	Some use of left leg.
	pm	Some use of left leg.
	13 am	Some use of left leg.
	pm	Some use of left leg.
	14 am	Some use of left leg.
	pm	Some use of left leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W24f (contd)	15 am	Some use of left leg.
	pm	Some use of left leg.
	16 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Normal faeces.
	17 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	18 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	19 am	Some use of left leg.
	pm	Some use of left leg.
	20 am	Some use of left leg.
	pm	Some use of left leg.
	21 am	Some use of left leg.
	pm	Some use of left leg.
	22 am	Some use of left leg.
	pm	Some use of left leg.
	23 am	Some use of left leg.
	pm	Some use of left leg.
	24 am	Some use of left leg.
	pm	Some use of left leg.
	25 am	Some use of left leg.
	pm	Some use of left leg.
	26 am	Some use of left leg.
	pm	Some use of left leg.
	27 am	Some use of left leg.
	pm	Some use of left leg.
	28 am	Some use of left leg.
	pm	Some use of left leg.
	29 am	Some use of left leg.
	pm	Some use of left leg.
	30 am	Some use of left leg.
	pm	Some use of left leg.
	31 am	Some use of left leg.
	pm	Some use of left leg.
	32 am	Some use of left leg.
	pm	Some use of left leg.
	33 am	Some use of left leg.
	pm	Some use of left leg.
	34 am	Some use of left leg.
	pm	Some use of left leg.
	35 am	Some use of left leg.
	pm	Some use of left leg.
	36 am	Some use of left leg.
	pm	Some use of left leg.
	37 am	Some use of left leg.
	pm	Some use of left leg.
	38 am	Some use of left leg.
	pm	Some use of left leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W24f	39 am	Some use of left leg.
	pm	Some use of left leg.
	40 am	Some use of left leg.
	pm	Some use of left leg.
	41 am	Some use of left leg.
	pm	Some use of left leg.
	42 am	Some use of left leg.
	pm	Some use of left leg.
	43 am	Some use of left leg.
	pm	Some use of left leg.
	44 am	Some use of left leg.
	pm	Some use of left leg.
	45 am	Some use of left leg.
	pm	Some use of left leg.
	46 am	Some use of left leg.
	pm	Some use of left leg.
	47 am	Some use of left leg.
	pm	Some use of left leg.
	48 am	Some use of left leg.
	pm	Some use of left leg.
	49 am	Some use of left leg.
	pm	Some use of left leg.
	50 am	Some use of left leg.
	pm	Some use of left leg.
	51 am	Some use of left leg.
	pm	Some use of left leg.
	52 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	53 am	Some use of left leg. Loose faeces.
	pm	Some use of left leg. Loose faeces.
	54 am	Some use of left leg.
	pm	Some use of left leg.
	55 am	Some use of left leg.
	pm	Some use of left leg.
	56 am	Some use of left leg.
	pm	Some use of left leg.
	57 am	Some use of left leg.
	pm	Sacrificed.
W466f	1 am	Alert and active. Not using right leg.
	pm	Alert and active. Not using right leg. Knee very swollen.
	2 am	Some use of right leg. Swelling on knee much reduced.
	pm	Some use of right leg.
	3 am	Some use of right leg.
	pm	Some use of right leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W466f (contd)	4 am	Some use of right leg.
	pm	Some use of right leg.
	5 am	Some use of right leg.
	pm	Some use of right leg.
	6 am	Some use of right leg.
	pm	Some use of right leg.
	7 am	Some use of right leg.
	pm	Some use of right leg.
	8 am	Some use of right leg.
	pm	Some use of right leg.
	9 am	Some use of right leg.
	pm	Some use of right leg.
	10 am	Some use of right leg.
	pm	Some use of right leg.
	11 am	Some use of right leg.
	pm	Some use of right leg.
	12 am	Some use of right leg.
	pm	Some use of right leg.
	13 am	Some use of right leg.
	pm	Some use of right leg.
	14 am	Some use of right leg.
	pm	Some use of right leg.
	15 am	Some use of right leg.
	pm	Some use of right leg.
	16 am	Swollen right knee.
	pm	Swollen right knee. Loose faeces.
	17 am	Swollen right knee. Loose faeces.
	pm	Swollen right knee. Loose faeces.
	18 am	Swollen right knee.
	pm	Swollen right knee.
	19 am	Swollen right knee.
	pm	Swollen right knee.
	20 am	Some use of right leg.
	pm	Some use of right leg.
	21 am	Some use of right leg.
	pm	Some use of right leg.
	22 am	Some use of right leg.
	pm	Some use of right leg.
	23 am	Some use of right leg.
	pm	Some use of right leg.
	24 am	Some use of right leg.
	pm	Some use of right leg.
	25 am	Some use of right leg.
	pm	Some use of right leg.
	26 am	Some use of right leg.
	pm	Some use of right leg.
	27 am	Some use of right leg.
	pm	Some use of right leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
W466f (contd)	28 am	Some use of right leg.
	pm	Some use of right leg.
	29 am	Some use of right leg.
	pm	Some use of right leg.
	30 am	Some use of right leg.
	pm	Some use of right leg.
	31 am	Some use of right leg.
	pm	Some use of right leg.
	32 am	Some use of right leg.
	pm	Some use of right leg.
	33 am	Some use of right leg.
	pm	Sacrificed.
X32f	1 am	Quiet. Not using left leg.
	pm	Quiet. Not using left leg.
	2 am	Some use of left leg.
	pm	Some use of left leg.
	3 am	Some use of left leg.
	pm	Some use of left leg.
	4 am	Some use of left leg.
	pm	Some use of left leg.
	5 am	Some use of left leg.
	pm	Some use of left leg.
	6 am	Some use of left leg.
	pm	Some use of left leg.
	7 am	Some use of left leg.
	pm	Some use of left leg.
	8 am	Some use of left leg.
	pm	Some use of left leg.
	9 am	Some use of left leg.
	pm	Some use of left leg.
	10 am	Some use of left leg.
	pm	Some use of left leg.
	11 am	Some use of left leg.
	pm	Some use of left leg.
	12 am	Some use of left leg.
	pm	Some use of left leg.
	13 am	Some use of left leg.
	pm	Some use of left leg.
	14 am	Some use of left leg.
	pm	Some use of left leg.
	15 am	Some use of left leg.
	pm	Some use of left leg.
	16 am	Some use of left leg.
	pm	Some use of left leg.

APPENDIX 6

(Clinical signs - continued)

Animal no./sex	Day no.	Clinical signs
X32f (contd)	17 am	Some use of left leg.
	pm	Some use of left leg.
	18 am	Some use of left leg.
	pm	Some use of left leg.
	19 am	Some use of left leg.
	pm	Some use of left leg.
	20 am	Some use of left leg.
	pm	Some use of left leg.
	21 am	Some use of left leg.
	pm	Some use of left leg.
	22 am	Some use of left leg.
	pm	Some use of left leg.
	23 am	Some use of left leg.
	pm	Some use of left leg.
	24 am	Some use of left leg.
	pm	Some use of left leg.
	25 am	Some use of left leg.
	pm	Some use of left leg.
	26 am	Some use of left leg.
	pm	Some use of left leg.
	27 am	Some use of left leg.
	pm	Some use of left leg.
	28 am	Some use of left leg.
	pm	Some use of left leg.
	29 am	Some use of left leg.
	pm	Some use of left leg.
	30 am	Some use of left leg.
	pm	Some use of left leg.
	31 am	Some use of left leg.
	pm	Some use of left leg.
	32 am	Some use of left leg.
	pm	Some use of left leg.
	33 am	Some use of left leg.
	pm	Sacrificed.

EXPERIMENTAL PROCEDURE

ANIMAL SUPPLY

Donor animals

Transgenic piglets were selected from litters produced by the Sponsor under Project Licence No. PPL[redacted] Transgenic piglets supplied for the study were 7 - 21 days old and their weights in the range 3.0 to 3.6 kg.

Recipient animals

Wild-caught baboons (*Papio anubis*) were obtained through a UK commercial supplier [redacted] Their estimated age at transplantation was 2 to 4 years and their weights in the range 5.2 to 7.6 kg.

The animals used in this study were selected from stock held on the behalf of the Sponsor to undergo screening as suitable recipients. Based on the results of the prescreening investigations, animals were selected by the Sponsor for transplant (see **PRE-OPERATIVE INVESTIGATIONS**). Whilst animals of either sex were selected, there was no specific requirement to maintain a balanced sex-ratio, as other selection criteria were more important. Only data relating to those animals that underwent transplant is presented in this report.

ANIMAL MANAGEMENT

Piglets

On the day of transplant, selected animals were delivered to the Huntingdon Research Centre by the Sponsor.

Baboons

On arrival at the Huntingdon Research Centre, all animals were examined by a Veterinary Officer, received an intramuscular injection of [redacted] to eliminate tapeworm infestation and were allocated a unique colony number, which was tattooed under the right arm. Intrapalpebral tuberculin tests were performed soon after arrival. Due to the frequency of planned laboratory investigations and by virtue of the fact that these animals were immunosuppressed, intrapalpebral tuberculin testing was stopped following transplant.

The animals were housed individually in cages specifically designed to house non-human primates in clean and secure conditions. The animals were housed in cages measuring 78 cm wide, 103 cm deep and 230 cm high. The cages were constructed of a stainless steel framework and 'printboard' walls, shelves and ceiling, incorporating a squeeze-back system, food hopper, water bottle holder and a removable 2.5 × 2.5 cm grid floor. Under the front half of each cage was a removable tray which contained wood chippings (Gold Chips sawdust [redacted] for use as a litter/forage substrate. The cages were cleaned and litter replaced each day. Automatic drinking valves, for the supply of drinking water, were used and tested each day.

The room in which the animals were kept was as far as practicable isolated from external disturbances. The room temperature was maintained as far as possible in the range 20 to 26°C, using heat exchangers connected to hot water supplied from oil-fuelled boilers. Relative humidity was maintained as far as possible in the range 45 to 70%. The environment was governed by a computer controlled building management system which continuously monitored the temperature and humidity controls and the operational state of the air handling plant. Temperature and relative humidity were recorded using a Kent Clearspan recorder. During the study temperature was recorded in the range 20 - 23°C and relative humidity in the range 60 - 90%. The high relative humidities recorded in the animal unit were attributable to washing down of the floors. Artificial lighting was used and was controlled to give 12 hours of light and 12 hours of dark per 24 hours. Air extraction was via a balanced system designed to give fifteen air changes per hour.

The animals were housed in the [redacted]

FOOD AND WATER

Baboons were each offered 350 grams, of standard dry diet (Primate Diet; [redacted], daily. Three hundred and fifty grams were offered in the morning.. In the morning before feeding, the residue of the previous day was removed and weighed. All animals were starved overnight prior to operation.

Water was available at all times, Vitamin C (Blackcurrant, [redacted] and [redacted] vitamin B_{12} preparation, [redacted] were added to the drinking water on one day of each week.

There was no information available to the Study Director to indicate that any non-nutrient substance likely to influence the effect of the test substance could reasonably be expected to be present in the diet or the drinking water, both of which are routinely subjected to chemical analysis. Results of all the analyses were lodged in the Huntingdon Life Sciences Archives (Huntingdon).

Wholemeal bread and fresh fruit or vegetable produce was sometimes offered in order to enrich the environment and improve the interaction between the animals and their handlers.

STUDY DESIGN

All animals were considered on an individual basis. A total of 22 animals underwent heterotopic abdominal cardiac xenotransplantation. The Sponsor was responsible for categorising the reasons why animals were sacrificed (*ie* technical failure, xenograft rejection, *etc*).

All animals that underwent transplant received immunosuppressive treatment with a combination of [redacted] and [redacted] and [redacted]. Immunosuppressive treatment commenced on Day [redacted], the day of transplant being designated Day 0.

Details of donor-recipient pairings for the transplants undertaken and the dates on which they were performed are listed in **APPENDIX 1**. All recipient animals were identified by their unique Huntingdon Research Centre colony number.

The study was designed such that all animals initially followed a standard immunosuppressive protocol prior to and immediately following transplant. After a few days the immunosuppressive regime was then individually tailored for each animal, being based on the results of laboratory investigations and blood drug levels. Details of the immunosuppressive regimes applied to individual animals are presented in Appendix 3. The initial dosing regimes are summarised as follows:

[redacted] was initially administered as [redacted] by intramuscular injection on Days [redacted] and [redacted] at dosage levels of [redacted] and [redacted] Oral administration of [redacted] commenced on Day [redacted] at a dosage level advised by the Sponsor and was given by gavage as a split dose in the morning and late afternoon or evening.

[redacted] was initially administered by intravenous injection on Days [redacted] and [redacted] at dosage levels of [redacted] and [redacted] respectively. Thereafter [redacted] was administered either orally or intravenously at the discretion of the Sponsor.

[redacted] was administered by intravenous injection on Day [redacted] at a dosage levels of [redacted] at the time of transplant. Animals were then dosed orally with [redacted] at the same dosage level on Days [redacted] and [redacted] after which the dosage level was reduced daily by [redacted] increments until a dosage of [redacted] was reached. Thereafter animals continued at this level until advised by the Sponsor.

Rejection episodes were treated by high dose injections of [redacted] usually given for three days.

[redacted] was administered orally by gavage commencing on Day [redacted] The initial dosage and frequency of administration each day changed during the course of the study. For early animals (X237m, X200f, X223m, X241m and X227m), [redacted] was administered only once daily. For subsequent animals on the study undergoing transplant, the frequency was increased up to three times daily as advised by the Sponsor.

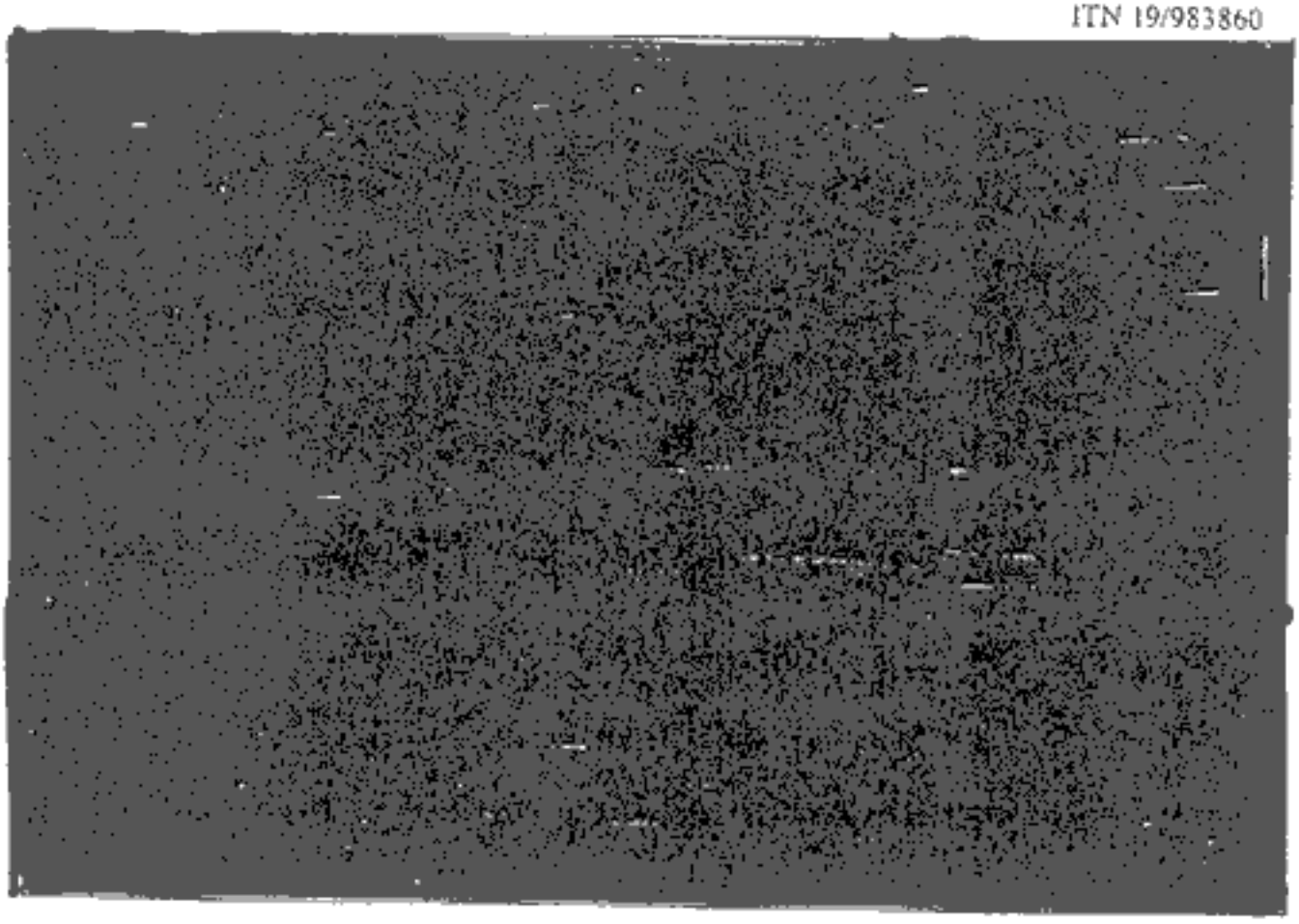
When administered on a single occasion each day, [redacted] was usually given in the afternoon. When administered on two occasions each day, [redacted] was usually given in the morning and again in the late afternoon/early evening. For those animals that received [redacted] three times daily, a third dose was administered late in the evening.

Transplant operations were performed on 1 or 2 recipient animals per day and were spread over a period of 22 weeks, dependent on the availability of surgical staff. The commencement of the study for these subgroups was therefore varied dependent on the date when the transplant(s) was performed.

The animals were housed in the [redacted]

PREPARATION OF THE IMMUNOSUPPRESSANTS

[redacted]



ADMINISTRATION OF THE TEST SUBSTANCES

The animals were dosed at approximately the same time(s) each day when applicable. Individual doses were adjusted according to the most recent bodyweight. The required quantity of each test solution was measured into a suitably graduated plastic syringe.

For oral dosing, the test solutions were administered through a plastic catheter [redacted] inserted *via* the mouth into the stomach. The catheter was flushed through with a small quantity (5/10 ml) of [redacted] (a high carbohydrate, low electrolyte, low fluid drink: [redacted]

For intravenous administration, the test solution was injected using a [redacted] infusion set inserted into the cephalic or saphenous vein.

For intramuscular administration, the test solution was injected through an appropriate gauge hypodermic needle. The animal was dosed in the thigh, the hair having been removed by clipping, to facilitate administration and to observe any local reaction to the injection.

Intravenous administration of steroid on the day of transplant was carried out during surgery. The dose was administered through an indwelling cannula inserted into a peripheral vein (cephalic or saphenous).

PRE-OPERATIVE INVESTIGATIONS

During the acclimatisation period, blood samples were obtained from potential recipient animals for investigations to enable the selection of the most compatible donor-recipient pairings for transplant. Blood samples were obtained for the following investigations.

Huntingdon Life Sciences:

1. Pre-study haematology and biochemistry

Imutran Limited:

2. Anti-pig antibody titres
3. CH50
4. Blood group

Investigations carried out on donor animals were the responsibility of the Sponsor and as such, have been documented and reported separately.

HETEROTOPIC CARDIAC TRANSPLANTATION

Cardiac transplantation in a primate weighing 3 - 5 kg is a procedure requiring microsurgical techniques. The donor and recipient animals were operated on simultaneously, thereby minimising the ischaemic time of the heart.

At the surgeon's discretion, various drug administrations may be made during the surgical procedure, which may be addition to those detailed in the protocol. Any such administrations were documented in the study records. Drugs given during the surgical procedure were normally administered intravenously unless stated otherwise int he protocol and/or study records.

Anaesthesia

Donor operation

The donor animal was sedated with [redacted] administered by intramuscular injection at a dosage of [redacted]. Anaesthesia was induced with [redacted] in a [redacted] mixture, delivered by a face mask. Following transfer to the operating table, a tracheotomy was performed to allow endotracheal intubation and mechanical ventilation was commenced. The animals was maintained on a [redacted] mixture and isoflurane at a concentration of [redacted]

Recipient operation

The animal was fasted for 8-12 hours prior to surgery (overnight). While still in its cage, the animal was given an intramuscular injection of [redacted] and [redacted]. Once sedated the animal was transferred to the operating suite. The neck area was shaved. A cannula was inserted into the saphenous vein and an intravenous injection of [redacted] given. An endotracheal tube was inserted and the animal maintained on O_2 with the addition of [redacted] at a concentration o[redacted]

Surgical procedure

Donor animal

The thoracic skin was prepared and draped to expose the operative field and a median sternotomy was performed to expose the intra-thoracic organs. The sternal halves were separated by a retractor and a thymectomy performed to allow better access to the pericardium, which was opened in the midline. At this stage the pig was heparinised systemically by direct injection of sodium heparin [redacted] into the superior vena cava. Dissection was performed to mobilise the heart and great vessels, passing slings around the intra-pericardial inferior vena cava (IVC), the superior vena cava (SVC), and the ascending aorta. The azygos vein was isolated and divided between ligatures as it enters the posterior aspect of the IVC. At this stage the heart was adequately mobilised for removal.

The ascending aorta was then cross clamped and cold crystalloid cardioplegic administered into the aortic route to institute cardioplegic arrest with exsanguination for the animal through the IVC and inferior pulmonary veins which were cut to allow drainage. After arrest was established the heart was excised by dividing in turn the IVC, left inferior and superior pulmonary veins, the left and right pulmonary arteries, the SVC and finally the ascending aorta. The heart was then transferred to a bowl containing cold saline and prepared for implantation.

After inspection for a patent foramen ovale, and creation of an atrio-septal defect if one was not present, the IVC and SVC were sutured closed, Next the back wall of the left atrium was prepared and the orifices of the pulmonary veins obliterated. The heart was now ready for implantation and was transferred to the recipient operating table.

Recipient animal

The abdominal skin was prepared with aqueous based betadine solution, and sterile drapes applied to expose the operative field. A midline laparotomy was then performed and the abdominal viscera gently retracted to allow exposure of the abdominal aorta and inferior vena cava at a level below the renal arteries. These vessels were then prepared to receive the vascular anastomoses of the donor heart and rubber slings were then passed around the vessels to isolate them.

Vascular clamps were applied to the aorta and vena cava proximal and distal to the planned site of the anastomoses. A longitudinal venotomy and arteriotomy was made to allow direct end to side suture of the donor pulmonary artery and aorta to the recipient vena cava and aorta respectively. Standard microvascular suture techniques were used. On completion of the anastomoses and before the sutures were finally tied the vessels were flushed with heparinised saline and back bleeding and forward flush techniques used to ensure that there was no thrombotic material within any of the vessels. After this flush the vascular clamps were removed to reperfuse the transplanted heart and the time recorded. Tissue glue [redacted] was placed around the anastomoses.

Once the surgeon was satisfied that there is stable xenograft function and adequate haemostasis is observed the abdominal wound was closed and the recipient allowed to recovery from general anaesthesia. The animal was then returned to its cage.

POST-OPERATIVE MANAGEMENT

Recipient animals were closely monitored for the first 24 hours post-operation. Heat lamps and/or thermostatic electric fan heaters were used to keep the animals warm until such time their use was no longer required, as determined by the attending veterinarian.

Post-operative analgesia was provided by the use of [redacted] which was administered at the discretion of the attending veterinary surgeon. Other drugs were also prescribed if considered appropriate. Details of individual drug administrations were recorded in the study records.

Animals received a single administration of [redacted] on the day prior to transplant. From Day 1, a single dose was given daily (or more frequently if considered necessary) at the discretion of the attending veterinarian. Animals received a subcutaneous dose at a dosage of [redacted]

Dependent on the clinical condition of each animal, food and/or fluid supplements may have been given at the discretion of the attending veterinary surgeon and/or Sponsor's monitoring scientist (or their deputy).

In the event of any animal showing a deterioration in it's clinical condition, heat lamps were used at the discretion of the attending HRC veterinarian.

POST-OPERATIVE OBSERVATIONS

Dated and signed records of all activities relating to the day by day running and maintenance of the study within the animal unit, as well as to the group observations and examinations outlined in this protocol, were recorded in the Study Day Book. In addition, observations relating to individual animals made throughout the day were recorded.

The following observations were made during the course of the study:

Mortality

The circumstances of any death was recorded in detail and a full *post mortem* examination was performed as described later. Prior to death, observations listed in this protocol were carried out, where practicable.

Clinical signs

All signs of ill health or reaction to treatment was recorded. Animals were checked regularly throughout the working day from approximately 0800 to 1700 hours (including weekends).

The animals were removed from their cages at regular intervals to assess their general condition and to palpate the transplanted heart to check for cardiac activity (see **POST-OPERATIVE INVESTIGATIONS**).

Bodyweight

The bodyweight of all animals was recorded generally weekly during the pre-operative period and daily during the post-operative period. The animals were weighed in the morning prior to dosing, or at a similar time during the pre-dosing period.

Food consumption

The quantity of food (standard dry diet) left by individual animals together with an estimate of the quantity spilled was recorded on a daily basis throughout the experimental period. From these data the quantities consumed were calculated.

POST-OPERATIVE INVESTIGATIONS

Xenograft function and physical examination

The functioning of the xenograft was determined as a minimum at least three times each day (approximately 0900, 1600 and 2200) for the first 2 weeks following transplant and then twice daily (approximately 0900 and 1700). Thereafter xenograft function was checked more frequently at the discretion of the Study Director and/or HRC veterinary staff. A check of the general physical condition of the animal was also performed at the same time.

If it was not possible to observe the xenograft functioning whilst the animal was in its cage, the animal was removed from its cage and the xenograft palpated, if necessary.

At these occasions additional treatments *ie* topical applications to wound, analgesics *etc*, may have been given to the animal as prescribed or directed by HRC's veterinarian or the Sponsor's representatives.

Blood sampling

Blood samples were obtained from each animal on the day prior to transplant (Day -1), the day of transplant (Day 0) and daily thereafter. The samples obtained and the investigations performed on them up to the first 15 days post-transplant were as shown overleaf:

Day	Volume	Investigation	Sample type
Day 1	0.5 ml	Anti-pig antibody	Plain
	0.5 ml	Anti-alpha-GAL	Plain
	0.5 ml	[redacted]assay	EDTA
	0.5 ml	Myocardial markers	Plain
Post Mycophenolate dosing:			
2 Hours	0.5 ml	[redacted]assay	EDTA
12 Hours	0.5 ml	[redacted]assay	EDTA
Day 0	1 ml	Held in immunology	Plain
	(0.5 ml aliquoted)	Myocardial markers	Plain
Day 1	0.5 ml	Myocardial markers	Plain
Mondays	0.3 ml	Haematology	EDTA
	0.7 ml	Biochemistry	Heparin
	0.5 ml	Myocardial markers	Plain
	0.5 ml	Anti-pig antibody	Plain
	0.5 ml	[redacted]	EDTA
	0.2 ml	[redacted]	EDTA
Tuesdays	0.3 ml	Haematology	EDTA
	0.5 ml	Anti-pigantibody	Plain
	0.5 ml	[redacted]	EDTA
Wednesdays	0.3 ml	Haematology	EDTA
	0.5 ml	Myocardial markers	Plain
	0.5 ml	Anti-pig antibody	Plain
	0.5ml	[redacted]	EDTA
	0.2 ml	[redacted]	EDTA
Thursdays	0.3 ml	Haematology	EDTA
	0.5 ml	Anti-pig antibody	Plain
	0.5 ml	[redacted]	EDTA
Fridays	0.3 ml	Haematology	EDTA
	0.5 ml	Myocardial markers	Plain
	0.5 ml	Anti-pig antibody	Plain
	0.5 ml	[redacted]	EDTA
	0.2 ml	[redacted]	EDTA
Saturdays	0.3 ml	Haematology	EDTA
	0.5 ml	Anti-pig antibody	Plain
	0.5 ml	[redacted]	EDTA
Sundays	0.3 ml	Haematology	EDTA
	0.5 ml	Anti-pig antibody	Plain
	0.5 ml	[redacted]	EDTA

The frequency of the haematology and biochemistry investigations was subsequently reduced to 3 times per week (Mondays, Wednesdays and Fridays) and all other samples reduced at the Sponsor's discretion, depending upon the general clinical condition of the animal.

Investigation of parameters additional to those listed in the original protocol were occasionally requested by the Sponsor's Monitoring Scientist and are detailed overleaf.

(a) **Laboratory investigations performed at HRC**

Haematology and biochemistry investigations performed as follows:

Haematology

	Units
300 µl into 0.5 ml EDTA tube. The following investigations were performed with a Bayer-Technicon H1E haematology analyser:	
Packed cell volume (PCV)	%
Haemoglobin (Hb)	g/dl
Red blood cell count (RBC)	$\times 10^{12}$/l
Total white cell count (WBC Total)	$\times 10^{9}$/l
Platelet count (Plts)	$\times 10^{9}$/l
Differential WBC count	
Neutrophils (N) Lymphocytes (L) Eosinophils (E) Basophils (B) Monocytes (M) Large unstained cells (LUC)	$\times 10^{9}$/l

Cell Morphology : If definitely abnormal cells were observed when examining any stained slide, such as the presence of Heinz bodies or abnormal lymphocytes, their presence or absence on each such slide examined was recorded and tabulated separately.

Biochemistry

700 µl into heparinised microtainer. The following parameters were analysed with a Hitachi 737 Clinical Chemistry analyser:	
Creatinine (Creat)	mg/dl
Sodium (Na)	mEq/l
Potassium (K)	mEq/l
Calcium (Ca)	mEq/l
Inorganic Phosphorus (P)	mEq/l

	Units
Chloride (Cl)	mEq/l
* Urea	mg/dl
* Total Bilirubin (Bili)	mg/dl
* Total Protein	g/dl
* Albumin	g/dl
* Alkaline Phosphatase (AP) Reaction temperature 30°C	mU/ml
* Glutamic-pyruvic transaminase (GPT), also known as 'Alanine aminotransferase' Reaction temperature 30°C	mU/ml
* Glutamic-oxaloacetic transaminase (GOT), also known as 'Apartate aminotransferase' Reaction temperature 30°C	mU/ml
γGlutamyl Transferase (γGT) Reaction temperature 30°C	mU/ml

The following parameters were analysed using a Roche Cobas Centrifugal analyser, using the appropriate BCL test kit:

* Leucine aminopeptidase (LAP) Reaction temperature 30°C	mU/ml
* Lactate dehydrogenase (LDH) Reaction temperature 30°C	mU/ml
* Creatine Phosphokinase (CPK) Reaction temperature 30°C	mU/ml
* Amylase Reaction temperature 37°C	mU/ml
* Uric acid Reaction temperature 30°C	mg/dl

The following parameters were analysed as described:

* Ornithine Corbamoyl transferase (OCT) - Method of Ceriotti, G. (Clin. Chim. Acta. 1973, 47, 97) Reaction temperature 37°C	mU/ml

	Units
* Osmolality (Osmo) Wescor vapour-pressure osmometer	mOs/kg
* Faecal occult blood (FOB) Using Ohokit (Hughes & Hughes)	-ve or +ve (secs)

* These parameters were only investigated for individual animals if indicated by their clinical condition and as recommended by the Sponsor or attending Veterinarian.

(b) **Blood samples despatched to Sponsor or other laboratories**

Anti-pig antibody levels

0.5 ml into plain tube. Samples were analysed at [redacted] for analysis.

[redacted]

0.2 ml into 0.5 ml EDTA tube. Samples were analysed at [redacted] for analysis.

Anti-αGAL assay

0.5 ml into plain tube. Samples were despatched to [redacted] for analysis.

Myocardial markers

0.5 ml into plain tube. Samples were despatched to [redacted] for analysis.

[redacted]

0.5 ml into EDTA tube. Samples were despatched to [redacted] Tooting, for analysis.

Blood samples were normally despatched on the day they were taken. At weekends or on weekdays when despatch was not undertaken the samples were centrifuged and the plasma or serum separated and stored in cardice.

TERMINAL STUDIES

The animals were maintained and dosed according to the immunosuppressive protocol unless sacrifice was required due to one of the following events occurring.

1. rejection of xenograft, as defined by absence of palpable cardiac activity.

2. opportunistic infection, as a result of the immunosuppressive treatment. Any signs of infection were brought to the attention of HRC veterinary staff and was treated symptomatically as considered necessary. In the event of an animal developing an infection that could not be treated, the animal was sacrificed following authorisation by the attending veterinarian.

3. drug toxicity, arising from the immunosuppressive treatment. Regular monitoring of the animals both clinically and by blood sampling minimised the risk of drug toxicity.

4. wound breakdown.

The Sponsor was contacted before any decision was taken to sacrifice an animal.

Pre-terminal blood sampling

Prior to sacrifice as much blood as practicable was collected and divided appropriately into heparinised and plain blood tubes.

Following centrifugation the plasma/serum was separated and deep frozen (in cardice) prior to despatch to the Sponsor for analysis.

Necropsy procedure

Each animal was immobilised with [redacted] given by the intramuscular route. A marrow sample was then obtained by sternal puncture and a smear prepared. The slide was allowed to dry in air and was then fixed in ethanol. The slide was despatched to the Sponsor with the other tissue samples on completion of the *post mortem*. The animals were then killed by a lethal dose of [redacted] and then rapidly exsanguinated by incision of the carotid blood vessels.

Immediately after exsanguination the xenograft with its associated anastomoses was carefully removed and weighed. A small section from the wall of each of the four chambers was taken and placed on a cork disc, covered in OCT-embedding matrix [redacted] and rapidly frozen in liquid nitrogen. Each section was then individually wrapped in foil and stored deep frozen in cardice, prior to despatch to the Sponsor. In addition, two pieces were collected into cryovials, frozen in liquid nitrogen and stored deep frozen in cardice.

The brain was removed and after the samples for virus studies had been taken, was placed in neutral buffered formalin.

Samples of spleen were taken as follows:

- two pieces were collected into cryovials and frozen in liquid nitrogen

- two pieces of spleen were placed on cork discs, covered in OCT-embedding matrix and rapidly frozen in liquid nitrogen. Each piece was then wrapped in foil.

Frozen samples were stored in cardice. All samples were despatched to the Sponsor.

Virus studies

Samples of the following tissues were required from all recipient animals where the cardiac xenograft had survived in excess of 5 days. The size of the sample was ideally approximately 0.5 cm^3 or if this size was not possible, as much was feasible. The samples were taken in triplicate, except for the xenograft where six pieces were taken.

- transplanted heart
- vascular anastomoses (junction or donor pulmonary artery and aorta and recipient vena cava and aorta
- lining of abdominal cavity that had been in contact with the transplanted heart
- kidney
- heart (recipient)
- lung
- liver
- ovaries or testes
- pancreas
- brain
- ileum
- mid-colon
- sternum
- spleen
- regional draining lymph nodes (mesenteric and retroperitoneal lymph nodes)
- plasma

All samples were snap frozen in liquid nitrogen and stored deep frozen in cardice prior to despatch to the Sponsor. Other non-routine tissues taken at the request of the Sponsor's Monitoring Scientist were documented in the study records.

LOCATION OF STUDY RECORDS

All specimens (except those sent to the Sponsor or other third party), raw data and other documents generated at Huntingdon Life Sciences, together with a copy of the final report were lodged in the Huntingdon Life Sciences, Archives, Huntingdon, England.

Such specimens and records will be retained for a minimum period of five years from the date of issue of this final report. At the end of the five year retention period the Client will be contacted and advice sought on their future requirements. Under no circumstances will any item be discarded without the Client's knowledge.

Data arising from any investigations made by the Sponsor or other third party, the findings of which are included in the Huntingdon Life Sciences final report, was retained and archived by the Sponsor.

PROCEDURES

The procedures used during the study, except those associated with heterotopic cardiac transplantation, were documented in the relevant Huntingdon Life Sciences Procedures Manuals.

DEVIATIONS FROM PROTOCOL

Review of the protocol by Huntingdon Life Sciences Quality Assurance Department noted the following points:

1. The protocol (page 2) states that this study will be performed under Home Office Project Licence number PPL 80/00848, 19b Procedure reference number 12. The Procedure reference number, however, is incorrect and should be stated as reference number 10.

2. The protocol (page 6) states that the weights of the transgenic piglets to be used for this study are expected to be in the range 5 - 8 kg. The weights of the animals used for the study were, however, in the range 2 - 3 kg.

3. The protocol (page 7) incorrectly stated that [redacted] was to be administered on Day [redacted] when in fact it should have been administered on Day [redacted] The details in Appendix 3 (proposed dosing schedule to Day 28) were, however, correct.

The following principal deviations from the protocol, not related to the clinical management of individual animals, should be noted:

1. The protocol (page 8) indicated that [redacted] would be administered daily by oral gavage at a dosage of [redacted] This regime was followed initially for the first few animals on the study (X237m), X200f, X223m and X241m), but was amended by the Sponsor, generally from Day [redacted] For animals X227m, X231m and X236f the starting dosage (Day [redacted] was increased by the Sponsor to [redacted]. For all subsequent animals allocated for transplant the frequency of dosing was increased up to three times daily, with the animals commencing dosing on Day -1 at [redacted]. When administered twice daily, [redacted] was usually given in the morning and again in the late afternoon/early evening. For those animals that received [redacted] three times daily, a third dose was administered late in the evening.

2. The requirements for blood samples for various investigations by the Sponsor were subject to frequent revision during the early stages of the study. Apart from changing the frequency of the blood sampling the number of blood samples required increased from that stated in the protocol until a more definitive blood sampling regime was notified by the Sponsor. This covered the blood sampling from Day -1 and for the first 15 days post-transplant. It also formed the default requirements thereafter. A copy is appended to this File Note. For purposes of reporting the blood samples indicated as being required for [redacted] have been described as myocardial markers. Serial blood sampling for [redacted] blood levels on Day -1 (0, +2 and +12 hours after the first dose) was introduced for animals X231m and X236, but did not become a routine feature of the study until animals X238f and X225m and those that followed afterwards. The protocol (page 16) indicated that the blood samples for [redacted] levels should be sent to [redacted] for analysis. The Sponsor subsequently requested that the samples be sent to [redacted] which became effective from 30 November 1996.

Whilst these deviations from the protocol were not formally documented by a Protocol Amendment, their performance is evident from the study records held by Huntingdon Life Sciences or the Sponsor. As such the Study Director does not consider that this omission had any significant impact on the integrity or outcome of the study.

APPENDIX 10

Individual clinical signs

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day the signs are considered to be unrepresentative of the underlying condition of each animal. Additionally, comments in the daybook by the veterinary officer or the Study Director are also reported.

2. Clinical signs are reported from the day following transplant (Day 1), except where the animal was sacrificed on the day of transplant.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X237m	0	am	Heart non-viable. Sacrificed in theatre.
X200f	1	am	Alert and active, looks bright. No faeces seen.
		pm	Alert and active. No faeces seen.
	2	am	Quiet but alert, fairly active. Normal faeces. General anaesthetic administered for repair of wound breakdown.
		pm	Quiet but alert, occasionally active, normal faeces. Found with large protrusion from wound. Transplanted heart beating well.
	3	am	Quiet but alert, appeared weak when handled. No faeces seen.
		pm	Quiet and huddled but alert, sitting on cage floor. No faeces seen. Later sitting on perch. Transplanted heart beating well.
	4	am	Quiet but alert. No faeces seen. Wound looks normal. Transplanted heart beating well.
		pm	Quiet but alert, occasionally active. Loose faeces.
	5	am	Alert and active, looks reasonably bright, moves around when stimulated. Faeces passed.
		pm	Quiet but reasonably alert.
	6	am	Quiet but alert, sitting on cage floor, appears to be shivering.. Loose faeces
		pm	Very quiet, becomes more alert when observed. Some puffiness under eyes. Loose faeces
	7	am	Very quiet, becomes more alert when observed. Some puffiness under eyes. Loose faeces
		pm	Very quiet, becomes more alert when observed. Some puffiness under eyes. Loose faeces
	8	am	Quiet but alert, sitting on perch. Slight swelling under both eyes. Loose faeces.
		pm	Records not completed.
	9	am	Quiet and huddled but alert, sitting on perch. Pale liquid faeces, appears dehydrated..
		pm	Quiet, no movement, huddled on perch. Liquid faeces.
	10	am	Quiet but alert. Some puffiness around eyes. Liquid faeces.
		pm	Quiet but alert, appears more mobile than earlier. Liquid faeces.
	11	am	Quiet but alert, sitting on perch. Slight swelling around both eyes. Loose faeces.
		pm	Quiet but alert, occasionally active, sitting on perch. Slight swelling around both eyes. Loose faeces.
	12	am	Quiet but alert, occasionally active. Area around wound appears swollen. Slight swelling under both eyes. Loose faeces. Transplanted heart beating well.
		pm	Quiet but alert, occasionally active, occasionally foraging in tray. Area around wound appears swollen. Slight swelling under both eyes. Loose faeces.
	13	am	Quiet but alert, occasionally active. Slight swelling under both eyes. Normal faeces.
		pm	Quiet but alert, occasionally active. Slight swelling under both eyes.
	14	am	Alert and active. Loose faeces. Transplanted heart beating.
		pm	Quiet but alert. Swelling under both eyes. Normal faeces.
	15	am	Quiet but alert, sitting on perch. Swelling under both eyes. Loose faeces. Transplanted heart beating.
		pm	Quiet but alert. Loose faeces.
	16	am	Quiet but alert, sitting on perch. Swelling under both eyes. Loose faeces. Transplanted heart beating.
		pm	Quiet but alert, sitting on perch. Swelling under both eyes. No faeces seen.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X200f (contd)	17	am	Quiet but alert, occasionally huddled, reluctant to move, slow when moving. Swelling under both eyes. No faeces seen
		pm	Quiet but alert, occasionally huddled, reluctant to move, slow when moving. Swelling under both eyes. No faeces seen
	18	am	Quiet and huddled, occasionally alert, very pale. Sitting on perch, reluctant to move and appears slow and weak when moving. Swelling under both eyes. Abdomen appears swollen, wound weeping. Normal faeces.
		pm	Rectal temperature 38.2°C.
	19	am	Quiet but alert, occasionally huddled. Reluctant to move, appears weak when handled. Abdomen appears swollen, large abdominal wall abscess. Slight swelling under both eyes. Loose faeces.
		pm	Scarificed for humane reasons.
X223m	0	pm	Transplanted heart not beating. Sacrificed in theatre.
X241m	1	am	Quiet but alert, unusual posture, lying on perch. Becomes active when approached. Slightly unsteady. Dehydrated. No faeces seen. Vomit in cage.
		pm	Quiet but alert. No faeces seen.
	2	am	Quiet but alert. Faeces passed.
		pm	Quiet but alert. Loose faeces.
	3	am	Quiet but alert, sitting on perch. Liquid faeces.
		pm	Quiet but alert, occasionally huddled, sitting on perch. Liquid faeces.
	4	am	Quiet but alert, occasionally huddled, sitting on perch. Liquid faeces.
		pm	Transplanted heart stopped beating. Sacrificed.
X227m	1	am	Lying on front across perch, no movement, eyes closed. No faeces seen. Transplanted heart stopped beating.
		pm	Sacrificed.
X231m	1	am	Alert and active. Normal faeces.
		pm	Alert and active.
	2	am	Quiet but alert, occasionally active. Slight oedema around wound.
		pm	Quiet but alert, occasionally active. Slight oedema around wound. Transplanted heart beating.
	3	am	Quiet but alert, occasionally active. Slight oedema around wound. Vomit in cage.
		pm	Quiet but alert, occasionally active. Slight oedema around wound. Transplanted heart beating.
	4	am	Quiet but alert. Loose faeces.
		pm	Quiet but alert.
	5	am	Alert and active. Swelling at lower end of wound. Normal faeces. Small amount of vomit in tray.
		pm	Quiet but alert. No faeces seen.
	6	am	Quiet but alert. Loose faeces.
		pm	Quiet but alert. Normal faeces.
	7	am	Alert and active. Transplanted heart beating.
		pm	Alert and active.
	8	am	Alert and active.
		pm	Transplanted heart beating.
	9	am	Quiet but alert.
		pm	Quiet but alert.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X231m (contd)	10	am	Alert and active.
		pm	Alert and active. Transplanted heart beating.
	11	am	Quiet but alert.
		pm	Quiet but alert.
	12	am	Quiet but alert.
		pm	Vomited after iv dosing. Quiet, sitting on floor at back of cage.
	13	am	Quiet but alert, occasionally active.
		pm	Quiet but alert, occasionally active. Very unsteady on return to cage post dosing.
	14	am	Alert and bright, sitting on ladder. Active when approached.
		pm	Very quiet and huddled. Later alert, sitting on cage floor, gentle activity.
	15	am	Alert but huddled on perch, becomes more active when approached. Transplanted heart not visibly beating.
		pm	Sacrificed.
X236f	0	pm	Transplanted heart stopped beating. Sacrificed.
X230f	0	am	Transplanted heart non-viable. Sacrificed.
X235m	1	am	Alert and vocalising, gentle activity on perch. Reluctant to move.
		pm	Transplanted heart beating.
	2	am	Quiet but alert, sitting on perch. No faeces seen.
		pm	Quiet but alert, sitting on perch. Normal faeces
	3	am	Alert and active.
		pm	Alert and active.
	4	am	Quiet but alert.
		pm	Transplanted heart beating.
	5	am	Alert and fairly active.
		pm	Alert and active. Crouched posture and vocalising when observed.
	6	am	Alert but huddled.
		pm	Quiet but alert, occasional crouched posture.
	7	am	Alert and active, sitting on perch, vocalising.
		pm	Alert and active, sitting on perch, vocalising.
	8	am	Alert and active.
		pm	Alert and active.
	9	am	Quiet but alert.
		pm	Quiet but alert.
	10	am	Alert and active.
		pm	Quiet but alert. Piloerection. No faeces seen.
	11	am	Alert, sitting on perch. Normal faeces.
		pm	Alert, walking around cage. Transplanted heart beating.
	12	am	Alert, sitting on perch.
		pm	Alert, sitting on perch. Transplanted heart beating.
	13	am	Alert and active.
		pm	Alert and active.
	14	am	Quiet but alert.
		pm	Quiet but alert, sitting on perch.
	15	am	Quiet but alert.
		pm	Quiet but alert, sitting on perch. Transplanted heart beating.
	16	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert, sitting on perch.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X235m (contd)	40	am	Subdued, sitting on perch. Pale loose faeces.
		pm	Subdued, sitting on cage floor. Diarrhoea.
	41	am	Slightly subdued, sitting on perch. Loose faeces.
		pm	Records not completed.
	42	am	Alert and quite active. Normal faeces.
		pm	Quiet but alert, sitting on cage floor. No faeces seen.
	43	am	Alert, slight activity. Transplanted heartbeat undetectable. Normal faeces.
		pm	Quiet but alert, sitting on cage floor.
	44	am	Alert but slightly subdued, sitting on perch. Transplanted heart beat weak.
		pm	Sacrificed.
X225m	1	am	Alert and fairly active.
		pm	Alert and fairly active.
	2	am	Quiet but alert, occasionally active.
		pm	Quiet but alert, occasionally active.
	3	am	Quiet but alert. Large volume of bloody mucoid faeces.
		pm	Liquid faeces.
	4	am	Quiet but alert, sitting on perch. Liquid faeces.
		pm	Alert and sitting on perch. Transplanted heart beating.
	5	am	Alert and active. Loose/liquid faeces.
		pm	Alert and active. No faeces seen. Transplanted heart beating.
	6	am	Quiet but alert, sitting on perch. Loose/liquid faeces.
		pm	Quiet and huddled, sitting on perch. Loose faeces.
	7	am	Quiet but alert. Loose faeces.
		pm	Quiet, sitting on cage floor. No faeces seen. Later alert, sitting slightly huddled on perch. Normal faeces.
	8	am	Quiet but alert..
		pm	Quiet but alert. Loose faeces. Transplanted heart beating.
	9	am	Quiet but alert. Normal faeces. Swollen right arm around injection site, possible local infection. Rectal temperature 39.3°C.
		pm	Quiet, sitting at front of cage, reluctant to move, reluctant to use right arm. Loose faeces.
	10	am	Quiet, huddled at front of cage, becomes alert when stimulated. Slightly unsteady, reluctant to move. Little/no use of right arm. Normal faeces.
	10	pm	Quiet but alert, occasionally huddled. No use of right arm which appears swollen.
	11	am	Quiet but alert. Right arm badly swollen and bruised.
		pm	Quiet but alert. Right arm badly swollen and bruised.
	12	am	Quiet but alert. Right arm still swollen, skin broken and oozing blood.
		pm	Quiet but alert on perch. No faeces seen. Transplanted heart beating.
	13	am	Quiet and slightly huddled. Right arm swollen.
		pm	Quiet and huddled. Right arm swollen with large open wound, heavily bruised, not bleeding. Vomit during dosing. Transplanted heart beating.
	14	am	Quiet but alert, sitting at front of cage. Slow movement. Large open wound on right arm, discharging pus. Normal faeces.
		pm	Quiet but alert, moves when stimulated. Wound on right arm larger than observed earlier.
	15	am	Quiet and huddled, sitting on perch. Reluctant to use right arm. Further wound breakdown. Scarificed for humane reasons.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X238f	1	am	Alert and fairly active.
		pm	Alert and fairly active.
	2	am	Quiet but alert. Normal faeces.
		pm	Quiet but alert.
	3	am	Quiet but alert. Loose faeces.
		pm	Quiet, sitting at back of cage.
	4	am	Quiet but alert. Normal faeces.
		pm	Quiet but alert, sitting at back of cage. Transplanted heart beating.
	5	am	Alert and active.
		pm	Alert and active. Transplanted heart beating.
	6	am	Quiet but alert, sitting on perch. Vomit in cage, salivating.
		pm	Quiet but alert. Loose faeces.
	7	am	Quiet but alert, sitting at back of cage, vocalising. Loose faeces.
		pm	Quiet but alert, sitting at back of cage on floor. No faeces seen.
	8	am	Quiet but alert. Normal faeces.
		pm	Alert and active. Transplanted heart beating.
	9	am	Asleep on perch.
		pm	Alert and active.
	10	am	Alert and active.
		pm	Quiet and huddled at back of cage. Becomes alert when stimulated.
	11	am	Alert and active. Vocalising.
		pm	Alert and active.
	12	am	Quiet but alert, sitting at front of cage. Dark faeces.
		pm	Alert and active. Normal faeces. Transplanted heart beating.
	13	am	Alert, sitting on cage floor.
		pm	Alert, sitting on cage floor. Vocalising.
	14	am	Quiet and huddled, sitting on cage floor, becomes alert and active when stimulated.
		pm	Quiet but alert.
	15	am	Huddled but alert, sitting on perch. Vocalising.
		pm	Huddled but alert, sitting on perch. Vocalising. Transplanted heart beating.
	16	am	Quiet, huddled, becomes alert when observed.
		pm	Alert, sitting on perch.
	17	am	Alert and active. Loose/liquid faeces. Vomit in tray.
		pm	Alert and active. No faeces seen. Transplanted heart beating.
	18	am	Quiet but alert, occasionally active. Normal faeces.
		pm	Quiet but alert.
	19	am	Subdued but alert, slightly active.
		pm	Records not completed.
	20	am	Subdued but alert, slightly active.
		pm	Alert and active, moving around cage.
	21	am	Slightly subdued, sitting on perch. Vocalising.
		pm	Slightly subdued, sitting on perch. Vocalising. Transplanted heart beating.
	22	am	Alert and active.
		pm	Alert and active. No faeces seen.
	23	am	Alert and active. Normal faeces.
		pm	Quiet but alert.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X238f (cont)	24	am	Alert and active.
		pm	Quiet but alert, sitting on perch.
	25	am	Alert and active.
		pm	Quiet but alert, sitting on perch.
	26	am	Quiet but alert, occasionally huddled. Pale faeces.
		pm	Quiet but alert, occasionally huddled. Pale faeces.
	27	am	Quiet but alert. Salivating post dosing. Liquid faeces.
		pm	Quiet but alert. Normal faeces.
	28	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert, sitting on perch.
	29	am	Quiet but alert, sitting on perch, moves when stimulated.
		pm	Alert and active.
	30	am	Quiet but alert.
		pm	Quiet but alert
	31	am	Quiet but alert.
		pm	Quiet but alert.
	32	am	Alert.
		pm	Quiet but alert. Transplanted heart beating.
	33	am	Alert and fairly active. Vocalising.
		pm	Alert and fairly active. Vocalising.
	34	am	Alert and fairly active. Vocalising.
		pm	Records not completed.
	35	am	Alert and fairly active.
		pm	Quiet but alert. Vocalising.
	36	am	Fairly quiet but active when observed. Dark faeces.
		pm	Alert and active, occasionally quiet.
	37	am	Bright and alert, sitting on perch. Normal faeces. Transplanted heartbeat weak.
		pm	Sacrificed.
X207m	1	am	Quiet, huddled, sitting on cage floor. Vocalising. No faeces seen.
		pm	Quiet but alert.
	2	am	Quiet but alert.
		pm	Quiet but alert, fairly active.
	3	am	Alert and active.
		pm	Alert and active.
	4	am	Alert and active. Vomit in tray
		pm	Quiet but alert, seems cold. Liquid faeces.
	5	am	Quiet but alert. Loose/liquid faeces.
		pm	Alert and active. Loose faeces.
	6	am	Quiet but alert. Vocalising. Normal faeces.
		pm	Alert and active. Transplanted heart beating.
	7	am	Quiet but alert, moving about cage.
		pm	Quiet but alert, moving about cage. Transplanted heart beating.
	8	am	Quiet but alert. Loose faeces.
		pm	Quiet but alert. Normal faeces.
	9	am	Quiet but alert. Loose faeces.
		pm	Quiet but alert. Loose faeces. Transplanted heart beating.
	10	am	Quiet but alert. Normal faeces.
		pm	Quiet but alert, sitting on perch.
	11	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert, sitting on perch, active if stimulated.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X207m (cont)	11	am	Quiet but alert, sitting on perch..
		pm	Quiet but alert, sitting on perch, active if stimulated. Transplanted heart beating .
	12	am	Quiet but alert, occasionally active.
		pm	Quiet but alert, occasionally active.
	13	am	Quiet but alert, slightly active. Profuse liquid faeces, shows abdominal discomfort.
		pm	Quiet but alert, sitting on cage floor. No faeces seen.
	14	am	Slightly subdued, sitting on perch. No faeces seen.
		pm	Slightly subdued, sitting on perch. No faeces seen.
	15	am	Quiet but alert and active. Sitting on perch. Dark faeces.
		pm	Transplanted heart beating.
	16	am	Quiet but alert. No faeces seen.
		pm	Alert and active, sitting on perch. Normal faeces.
	17	am	Alert, bursts of activity. Thinning of body hair.
		pm	No comment recorded
	18	am	Quiet but alert.
		pm	Quiet but alert, sitting on perch.
	19	am	Quiet but alert.
		pm	Quiet but alert, sitting on perch.
	20	am	Quiet but alert. Loose faeces.
		pm	Quiet but alert. Normal faeces.
	21	am	Quiet but alert, reluctant to move.
		pm	Quiet but alert, sitting on perch, reluctant to move, active if stimulated. Transplanted heartbeat feels faint.
	22	am	Quiet but alert, sitting on perch, moves slowly if stimulated.
		pm	Quiet but alert. Bloody discharge from penis.
	23	am	Quiet but alert, sitting on perch.
		pm	Quiet.
	24	am	Quiet but alert.
		pm	Quiet but alert.
	25	am	Quiet but alert.
		pm	Quiet but alert. Transplanted heart not beating.
	26	am	Sacrificed.
X228f	0	pm	No heartbeat from transplanted heart. Sacrificed.
X211m	1	am	Slightly subdued. Normal faeces.
		pm	Quiet, appears asleep leaning against front of cage, reluctant to move. Slight oedema around wound. No faeces seen.
	2	am	Quiet.
		pm	Appears asleep at front of cage, becomes alert when approached. Normal faeces.
	3	am	Quiet but alert.
		pm	Quiet but alert, occasionally huddled.
	4	am	Quiet but alert, sitting on perch, moves slowly when stimulated.
		pm	Quiet but alert and active at times. No faeces seen.
	5	am	Quiet but alert, sitting on perch, moves slowly when stimulated. Normal faeces. Retching and salivating.
		pm	Quiet but alert, sitting on perch, moves slowly when stimulated.
	6	am	Alert and active.
		pm	Alert.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X211m cont	7	am	Alert and active.
		pm	Quiet, sitting on perch, moves slowly when stimulated.
	8	am	Alert and active, sitting on perch
		pm	Quiet but alert.
	9	am	Quiet but alert, sitting on perch, becomes active when approached.
		pm	Quiet but alert, sitting on perch, becomes active when approached. Transplanted heart beating well.
	10	am	Alert, sitting on perch.
		pm	Alert and active.
	11	am	Quiet, huddled on perch.
		pm	Quiet but alert, no faeces seen. Transplanted heart beating well.
	12	am	Alert and active. Vocalising.
		pm	Slightly subdued, sitting on perch.
	13	am	Quiet but alert, occasionally active.
		pm	Quiet but alert, occasionally active.
	14	am	Slightly subdued, occasionally active.
		pm	Slightly subdued, occasionally active.
	15	am	Quiet but alert, active at times.
		pm	Quiet but alert, active at times. Transplanted heart beating well.
	16	am	Quiet but alert.
		pm	Quiet but alert, occasionally active.
	17	am	Quiet but alert.
		pm	Quiet but alert.
	18	am	Quiet but alert.
		pm	Quiet but alert. Transplanted heart beating well.
	19	am	Quiet but alert.
		pm	Quiet but alert.
	20	am	Quiet but alert.
		pm	Alert and active.
	21	am	Alert, moving around cage, occasionally quiet.
		pm	Quiet, slightly active.
	22	am	Quiet but alert, occasionally active.
		pm	Quiet but alert, occasionally huddled.
	23	am	Quiet but alert, occasionally foraging in tray.
		pm	Quiet but alert, occasionally foraging in tray.
	24	am	Quiet, occasionally huddled.
		pm	Quiet and huddled but alert. No faeces seen. Vomit in tray.
	25	am	Alert, moving around cage. Dark faeces.
		pm	Quiet and huddled, becomes alert when stimulated. Normal faeces.
	26	am	Quiet but alert. Some puffiness around eyes.
		pm	Quiet and huddled, becomes alert when stimulated. Transplanted heart beating
	27	am	Quiet but alert. Eyes normal.
		pm	Quiet but alert. No faeces seen.
	28	am	Subdued and huddled on perch. Loose faeces.
		pm	Quiet and huddled, becomes alert when approached, reluctant to move. No faeces seen.
	29	am	Quiet and huddled but alert. Normal faeces
		pm	Quiet, slow to react, sitting on perch.
	30	am	Slightly subdued, huddled on perch.
		pm	Quiet and huddled, reluctant to move. Vomited post dosing.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X211m (contd)	31	am	Slightly subdued, sitting on perch. Loose faeces. Transplanted heartbeat weak.
		pm	Quiet but alert, occasionally huddled, reluctant to move. No faeces seen. Transplanted heart feels hard to touch and contractions faint.
	32	am	Subdued. Normal faeces. Transplanted heartbeat very weak.
		pm	Alert and active. Loose faeces. Sacrificed.
X214f	1	am	Slightly subdued. No faeces seen.
		pm	Quiet but alert, moves when stimulated.
	2	am	Alert.
		pm	Quiet but alert, resting against cage front, moves when approached. No faeces seen.
	3	am	Quiet and huddled but alert, appears weak. Normal faeces.
		pm	Quiet and huddled, sitting on cage floor, reluctant to move. No faeces seen.
	4	am	Quiet and huddled, pale mucous membranes, sitting on cage floor, appears weak when moving. Abdomen appears slightly swollen. No faeces seen.
		pm	Quiet and huddled. Normal faeces.
	5	am	Collapsed on cage floor. Abdomen swollen and appears fluid filled. Salivating. Very laboured breathing. Extreme difficulty trying to walk. Pale mucous membranes. Loose faeces. Scarificed for humane reasons.
X217m	1	am	Quiet but alert, sitting on perch. Small amount of faeces seen.
		pm	Quiet but alert. Small amount of faeces seen.
	2	am	Quiet and heavy lidded, sitting on perch, resting against front of cage, reluctant to move. Small amount of normal faeces.
		pm	Quiet but alert, occasionally active. Loose faeces.
	3	am	Quiet, reluctant to move.
		pm	Quiet but alert. Normal faeces.
	4	am	Quiet, reluctant to move, lying in corner of cage.
		pm	Quiet but alert, sitting on perch.
	5	am	Quiet but alert.
		pm	Quiet but alert. Transplanted heart stopped beating. Sacrificed.
X204f	1	am	Quiet but alert, occasionally heavy lidded, reluctant to move. Small amount of faeces seen.
		pm	Subdued, sitting on cage floor, occasionally laying down, becomes alert when stimulated but reluctant to move. Mucous membranes slightly pale. Transplanted heart pulse relatively strong. Normal faeces.
	2	am	Quiet but alert, sitting on perch, reluctant to move. Liquid faeces.
		pm	Quiet but alert, occasionally active. Loose faeces.
	3	am	Quiet but alert.
		pm	Quiet, huddled but alert. Normal faeces.
	4	am	Quiet but alert. Slightly loose dark faeces.
		pm	Quiet but alert, sitting on perch. No faeces seen.
	5	am	Quiet but alert, periods of laying on cage floor. Normal faeces.
		pm	Transplanted heart stopped beating. Sacrificed.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X222m	1	am	Quiet but alert. Normal faeces.
		pm	Quiet but alert, sitting on perch. Died suddenly at 11.40 pm.
X229m	1	am	Unusual posture. No faeces seen.
		pm	Quiet but alert, sitting on perch. Vocalising. Loose faeces.
	2	am	Alert, fairly active. Normal faeces.
		pm	Quiet but alert, occasionally active. Normal faeces.
	3	am	Slightly subdued, sitting on perch. Loose/normal faeces.
		pm	Quiet but alert, moves when stimulated. Small amount of normal faeces.
	4	am	Alert and active if stimulated. Loose faeces.
		pm	Quiet but alert. Loose faeces.
	5	am	Quiet but alert. Normal faeces.
		pm	Slightly subdued, sitting on perch. No faeces seen.
	6	am	Quiet but alert. Normal faeces.
		pm	Slightly subdued, sitting on perch. No faeces seen.
	7	am	Quiet but alert, active in cage. Slightly loose faeces.
		pm	Quiet but alert, sitting on perch. Dark coloured liquid faeces.
	8	am	Quiet but alert, standing on perch. Dark loose faeces.
		pm	Slightly subdued, active if stimulated. Dark loose faeces. Later subdued and huddled on perch.
	9	am	Subdued. Salivating pre and post dosing. Slightly dehydrated. Liquid faeces.
		pm	Quiet and huddled. Salivating. No faeces seen. Transplanted heart beating well.
	10	am	Very subdued, heavy lidded, inactive even when stimulated. No faeces seen.
		pm	Transplanted heart stopped beating. Sacrificed.
X232f	0	am	No abnormalities detected. Transplanted heart not viable. Sacrificed in theatre.
X240f	1	am	Alert and active. No faeces seen.
		pm	Quiet but alert, sitting on perch. No faeces seen. Transplanted heart beating well.
	2	am	Quiet, eyes partially closed. Normal faeces.
		pm	Quiet but alert, sitting on perch. No faeces seen.
	3	am	Alert, fairly active. No faeces seen.
		pm	Quiet but alert, sitting on perch. Normal faeces.
	4	am	Bright, alert and active. No faeces seen.
		pm	Quiet but alert, active if approached.
	5	am	Alert and active. Normal faeces.
		pm	Alert and active. No faeces seen.
	6	am	Quiet but alert. Normal faeces.
		pm	Active, alert and responsive.
	7	am	Quiet but alert.
		pm	Alert and active.
	8	am	Quiet but alert and active.
		pm	Quiet but alert and active.
	9	am	Quiet but alert.
		pm	Quiet but alert and active, moving in cage.
	10	am	Alert, fairly active.
		pm	Alert, fairly active.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X240f cont	11	am	Alert and active.
		pm	Quiet but alert and active if stimulated.
	12	am	Quiet but alert and active if stimulated.
		pm	Alert and active.
	13	am	Alert and active.
		pm	Alert and active.
	14	am	Alert and active.
		pm	Alert and active.
	15	am	Alert and active if stimulated.
		pm	Alert and active.
	16	am	Quiet but alert and active if stimulated.
		pm	Quiet, active if stimulated.
	17	am	Quiet but alert and active if stimulated.
		pm	Alert and active.
	18	am	Alert but quiet.
		pm	Quiet but alert.
	19	am	Alert. Vocalising.
		pm	Alert.
	20	am	Quiet but alert.
		pm	Quiet but alert.
	21	am	Alert and active.
		pm	Alert and active.
	22	am	Quiet but alert.
		pm	Quiet but alert
	23	am	Quiet but alert, slightly active.
		pm	Quiet but alert, sitting on perch.
	24	am	Quiet but alert.
		pm	Quiet but alert.
	25	am	Quiet but alert and active, but slow movements.
		pm	Quiet but alert and active, but slow movements.
	26	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert, sitting on perch.
	27	am	Alert and active when observed.
		pm	Quiet but alert.
	28	am	Quiet but alert and active. Small soft gingival swelling.
		pm	Quiet but alert.
	29	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert.
	30	am	Quiet but alert, sitting on perch, becomes active when stimulated.
		pm	Quiet but alert. No faeces seen.
	31	am	Quiet but alert. Vomit in tray. Normal faeces.
		pm	No comment recorded
	32	am	Vomit in cage.
		pm	Quiet but alert, occasionally active.
	33	am	Alert.
		pm	Quiet but alert. Vomit in cage.
	34	am	Quiet but alert. Normal faeces.
		pm	Quiet but alert, occasionally active.
	35	am	Quiet but alert.
		pm	Quiet but alert. Transplanted heart beating well.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X240f (contd)	36	am	Quiet but alert, slow movements when active.
		pm	Quiet but alert, slow movements when active. Transplanted heart beating well.
	37	am	Alert and active.
		pm	Alert, sitting on perch. Transplanted heart beating well.
	38	am	Quiet but alert.
		pm	Alert, sitting on perch.
	39	am	Alert and active.
		pm	Alert and active.
	40	am	Quiet but alert, slow movements when occasionally active.
		pm	Alert, sitting on perch. No faeces seen.
	41	am	Quiet but alert, slow movements when active. Normal faeces.
		pm	Quiet but alert, sitting on perch. No faeces seen. Transplanted heart beating well.
	42	am	Quiet but alert, slow movements when active. Normal faeces.
		pm	Quiet but alert, slow movements when active.
	43	am	Quiet but alert.
		pm	Quiet but alert, slow movements when active.
	44	am	Quiet but alert.
		pm	Quiet but alert, sitting on perch.
	45	am	Quiet but alert.
		pm	Quiet but alert.
	46	am	Quiet but alert.
		pm	Quiet but alert.
	47	am	Quiet but alert. No faeces seen.
		pm	Quiet but alert. Normal faeces.
	48	am	Quiet but alert, clinging to cage front.
		pm	Alert and fairly active.
	49	am	Quiet but alert, slow movements when active.
		pm	Quiet but alert, slow movements when active. Transplanted heart beating well.
	50	am	Quiet but alert..
		pm	Quiet but alert.
	51	am	Quiet but alert.
		pm	Quiet but alert. Transplanted heartbeat irregular and slow, feels enlarged and hard.
	52	am	Quiet but alert.
		pm	Quiet but alert.
	53	am	Quiet but alert.
		pm	Quiet but alert.
	54	am	Quiet but alert.
		pm	Quiet but alert, reasonably active.
	55	am	Quiet but alert.
		pm	Quiet but alert.
	56	am	Quiet but alert.
		pm	Quiet but alert. Transplanted heart beating well. Position of heart mid-abdominal compared with lower-abdominal last week.
	57	am	Quiet but alert, fairly active.
		pm	Quiet but alert, fairly active.
	58	am	Quiet but alert, fairly active. Large vomit in cage.
		pm	Quiet but alert, fairly active. Transplanted heart beating well.
	59	am	Quiet but alert.
		pm	Quiet but alert, foraging in tray. Transplanted heart beating well.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X240 (cont)	60	am	Quiet but alert, foraging in tray.
		pm	Quiet but alert.
	61	am	Alert and reasonably active.
		pm	Alert and reasonably active.
	62	am	Alert and reasonably active. Slightly dark faeces.
		pm	Alert and reasonably active. Slightly dark faeces.
	63	am	Quiet but alert, fairly active. Normal faeces.
		pm	Quiet but alert, fairly active.
	64	am	Quiet but alert.
		pm	Quiet but alert. Transplanted heart beating well.
	65	am	Quiet but alert.
		pm	Alert and active.
	66	am	Alert and active.
		pm	Alert but quiet. No faeces seen. Vomit in cage.
	67	am	Quiet but alert, fairly active. Normal faeces. Small vomit in tray.
		pm	Quiet but alert, occasionally active. No faeces seen.
	68	am	Quiet but alert. Normal faeces.
		pm	Quiet but alert, fairly active.
	69	am	Quiet but alert, active when stimulated.
		pm	Quiet but alert, active when stimulated.
	70	am	Quiet but alert.
		pm	Quiet but alert.
	71	am	Quiet but alert.
		pm	Alert and active, moving around cage.
	72	am	Quiet but alert.
		pm	Quiet, sitting on perch.
	73	am	Quiet but alert, active in cage. Normal faeces.
		pm	Quiet on cage floor, but alert and active.
	74	am	Quiet but alert and active.
		pm	Quiet but alert and active.
	75	am	Alert and fairly active.
		pm	Alert and fairly active.
	76	am	Quiet but alert.
		pm	Quiet but alert.
	77	am	Quiet but alert, occasionally active.
		pm	Quiet but alert. Transplanted heart beating well.
	78	am	Quiet but alert.
		pm	Quiet but alert.
	79	am	Quiet but alert.
		pm	Quiet but alert. Transplanted heart beating well.
	80	am	Slightly subdued, moves slowly when stimulated.
		pm	Quiet but alert, fairly slow movement. Transplanted heart beating well.
	81	am	Quiet, eyes partially closed.
		pm	Quiet, huddled but alert. Appears tired and weak.
	82	am	Quiet but alert, seems very weak. Fine muscle tremors.
		pm	Quiet, huddled.
	83	am	Quiet but alert, seems tired. No muscle tremors.
		pm	Quiet, huddled. No faeces seen.
	84	am	Quiet but alert, sitting on perch. Normal faeces.
		pm	Quiet but alert, sitting on perch.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X240f (contd)	85	am	Quiet but alert, occasionally active.
		pm	Quiet but alert, occasionally active. Transplanted heart beating well.
	86	am	Subdued but alert, sitting on perch.
		pm	Subdued but alert, sitting on perch.
	87	am	Quiet but alert. Vomit in tray
		pm	Quiet, huddled on cage floor. No faeces seen. Transplanted heart beating well.
	88	am	Alert, sitting on perch. Normal faeces.
		pm	Sitting on cage floor, active when stimulated.
	89	am	Quiet and huddled, seems tired. Rectal temperature 40.6°C.
		pm	Quiet and huddled, seems tired, reluctant to move from perch.
	90	am	Quiet and huddled, seems tired. Rectal temperature - within normal range.
		pm	Quiet and huddled, seems tired. Rectal temperature - within normal range.
	91	am	Quiet but alert, occasionally active.
		pm	Quiet but alert, occasionally active.
	92	am	Quiet and huddled, reluctant to move. Exhibits discomfort when moving, especially right leg.
		pm	Quiet and huddled but alert, some movement seen.
	93	am	Quiet but alert, sitting on perch, seems to have difficulty walking.
		pm	Quiet but alert, sitting on perch.
	94	am	Quiet and huddled. Loose faeces.
		pm	Quiet but alert, not very active. Transplanted heart beating satisfactorily.
	95	am	Quiet and huddled on perch, reluctant to move. Body and head tremors. Normal faeces.
		pm	More alert and active than noted in the morning.
	96	am	Quiet and huddled on perch but alert, little movement. Some limb tremors.
		pm	Quiet and huddled on perch but alert, little movement. No faeces seen. Large vomit in cage.
	97	am	Quiet and huddled on perch. Vomit in tray. Normal faeces.
		pm	Quiet but alert, sitting on perch. transplanted heart beating satisfactorily.
	98	am	Quiet but alert, sitting on ladder. Reluctant to move. Normal faeces.
		pm	Quiet but alert, sitting on ladder. Seems unsteady at times.
	99	am	Quiet but alert. Normal faeces. Scarificed for humane reasons.
X226f	1	am	No comment recorded
		pm	Quiet but alert, moving around in cage. No faeces seen.
	2	am	Alert and fairly active. No faeces seen.
		pm	Alert and fairly active. No faeces seen.
	3	am	Subdued but alert.
		pm	Quiet but alert, sitting on ladder.
	4	am	Subdued but alert. Normal faeces.
		pm	Alert and fairly active. No faeces seen.
	5	am	Quiet and huddled but alert. Normal faeces.
		pm	Quiet and huddled but alert.
	6	am	Quiet and huddled but alert and active if stimulated..
		pm	Alert and active.
	7	am	Alert and active. No faeces seen.
		pm	Alert and active. Normal faeces.
	8	am	Quiet but alert. No faeces seen.
		pm	Quiet but alert, fairly active. Normal faeces.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X226f (cont)	9	am	Quiet but alert
		pm	Quiet but alert.
	10	am	Alert and active
		pm	Alert and active.
	11	am	Quiet but alert.
		pm	Quiet but alert.
	12	am	Quiet but alert.
		pm	Sacrificed

APPENDIX 10

Individual clinical signs

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following the transplant (Day 1) except when animal did not survive beyond Day 0.

APPENDIX 10

(Individual clinical signs - continued)

Animal No./sex	Day No.		Observation
X216f	1	am	Quiet but alert, sitting on perch. Normal faeces.
		pm	Quiet but alert, fairly active. No faeces seen.
	2	am	Alert, sitting on perch. Normal faeces.
		pm	Slightly subdued, sitting on perch.
	3	am	Alert, slow and laboured movement.
		pm	Alert, slow and laboured movement.
	4	am	Quiet but alert. Dark faeces.
		pm	Quiet and huddled. Yellowish coloured loose/liquid faeces.
	5	am	Quiet but alert, slow to react. Loose faeces. No detectable beat from transplanted heart. Sacrificed for humane reasons.
X218f	1	am	Alert but subdued, sitting on perch. No faeces.
		pm	Alert and active. No faeces.
	2	am	Pale, lying on cage floor.
		pm	Alert and active. Later subdued, sitting on cage floor, reluctant to move. Normal faeces.
	3	am	Quiet but alert. Loose faeces.
		pm	Quiet but alert, huddled on perch. No faeces.
	4	am	Quiet but alert, sitting on cage floor. Dark faeces.
		pm	Quiet but alert, sitting on cage floor, slow movements. Loose faeces.
	5	am	Quiet but alert, active when stimulated. Loosel faeces.
		pm	Quiet, sitting on cage floor, no movement. Loose faeces.
	6	am	Lying on cage floor, moves only when stimulated. Fluid around wound. Loose faeces.
		pm	Quiet but alert, active when stimulated.
	7	am	Quiet but alert, sitting on perch, not very responsive. Normal faeces.
		pm	Quiet but alert, sitting on perch.
	8	am	Quiet and huddled. Loose faeces.
		pm	Quiet and huddled. 22.50 found collapsed in cage with no detectable respiration or pulse. Sacrificed for humane reasons.
X224f	1	am	Alert and huddled but subdued. No faeces seen.
		pm	Quiet but alert, fairly active. Normal faeces.
	2	am	Alert and huddled but subdued.
		pm	Slightly subdued, moves when stimulated.
	3	am	Alert and active. Dark faeces.
		pm	Quiet but alert, huddled on cage floor. Loose faeces.
	4	am	Alert and active. Fluid around wound. Vomit on cage floor. Normal faeces.
		pm	Quiet but alert.
	5	am	Quiet but alert. Loose faeces.
		pm	Quiet but alert, active if stimulated. Loose faeces.
	6	am	Quiet but alert. Loose/liquid faeces.
		pm	Quiet but alert.
	7	am	Quiet but alert, sitting on perch. Normal faeces.
		pm	Quiet but alert and active.

APPENDIX 10

(Individual clinical signs - continued)

Animal No./sex	Day No.		Observation
X224f (contd)	8	am	Quiet and huddled. Loose faeces.
		pm	Quiet and huddled. No faeces seen.
	9	am	Quiet but alert, vocalising, occasionally active. Loose faeces.
		pm	Quiet but alert, vocalising, occasionally active. Loose faeces. 22.55 transplanted heart beating irregularly.
	10	am	Alert and active. Normal faeces. No detectable beat from transplanted heart. Sacrificed for humane reasons.
X220f	0	am	Quiet and huddled. Small vomit in tray.
		pm	No detectable beat from transplanted heart. Sacrificed for humane reasons.
X198f	1	am	Quiet and huddled, sitting on perch. Normal faeces. Sudden collapse, sitting on cage floor, reluctant to move, weak pulse and pale colour. Transplanted heart beating irregularly.
		pm	Quiet and lethargic, sitting on perch. Transplanted heart beating slowly and weakly.
	2	am	Quiet, unusual posture, slow movement, unsteady when stimulated, weak when handled. Frank haemorrhage from abdominal wound (possible slow haemorrhage from anastomosis). No faeces seen. Transplanted heart beating slowly and weakly. Sacrificed for humane reasons.

EXPERIMENTAL PROCEDURE

ANIMAL MANAGEMENT

A total of 6 young purpose-bred cynomolgus monkeys (2 males and 4 females) obtained from a commercial supplier [redacted] were allocated to this study. The animals were originally bred in Mauritius. Their ages at the start of the study were 16 to 31 months and their weights were in the range 1.8 to 2.3 kg.

The animals were conditioned for at least 4 weeks before delivery to the Huntingdon Life Sciences. Documentation received from the supplier included details relating to quarantine dates, health screening and any treatment administered during the conditioning period. On arrival at Huntingdon Life Sciences they were examined by a veterinary officer and allocated a unique colony number, which was tattooed under the right arm. Intrapalpebral tuberculin tests were performed. Prior to the start of dosing a review of animal health was undertaken by a veterinary officer.

The animals were housed individually in cages specifically designed to house primates in clean and secure conditions. The cages were constructed of aluminium and electro-polished stainless-steel, incorporating a squeeze-back system, food hopper, bottle holders and a 2.5 x 2.5 cm grid floor. The cages were changed at intervals of approximately 4 weeks. The cages were entirely wall-mounted in two tiers, each tier combined with an excreta removal flushing system which was cleaned twice daily after recording of food residues. Automatic drinking valves, for the supply of drinking water were used.

The room in which the animals were kept was relatively isolated from external disturbances. The room temperature was maintained in the range 16 - 23°C, using heat exchangers connected to hot water supplied from oil-fuelled boilers. Relative humidity was generally maintained in the range 30 - 80%. Although there were slight deviations outside the environmental conditions stated in the protocol, these were minor and were not considered to have had an effect on the integrity of the study. The environment was governed by a computer controlled building management system which continuously monitored the temperature and humidity controls and the operational state of all the air handling plant. Temperature and relative humidity were continuously recorded using a Cambridge Recorder. Artificial lighting was used and controlled to give 12 hours of light and 12 hours of dark per 24 hours. Air extraction was via a balanced system designed to give fifteen air changes per hour.

Each animal was offered 200 grams of standard dry diet (Primate Diet: [redacted] daily. One hundred grams was generally given approximately one hour after dosing, and a further 100 grams later in the working day. In the morning the residue of the meal from the previous day was removed and weighed before new food was offered.

Water was available at all times. Vitamic C, (Blackcurrant [redacted] and [redacted] a vitamin B_{12} preparation [redacted] were added to the drinking water on one day of Week 1 and daily thereafter.

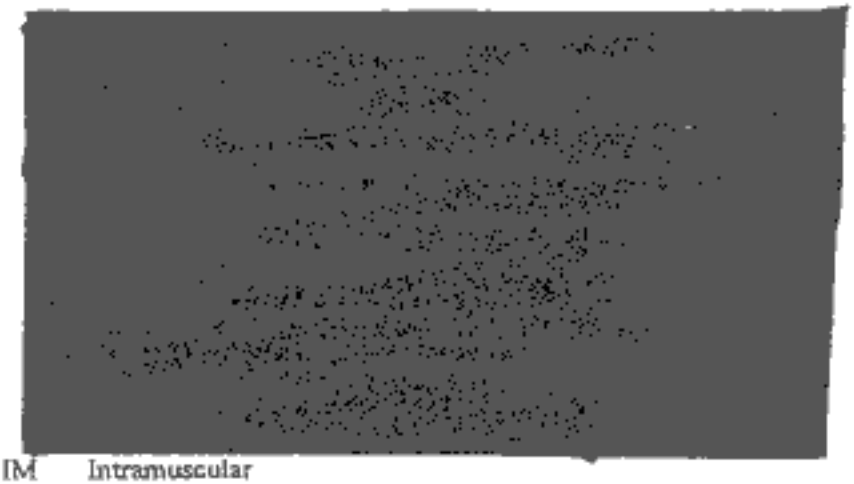
There was no information available to the Study Director to indicate that any non-nutrient substance likely to influence the effect of the test material could reasonably be expected to be present in the diet or the drinking water, both of which were routinely subjected to chemical analysis. Results of all the analyses are lodged in the Huntingdon Life Sciences Archives.

Wholemeal bread and fresh fruit or vegetable produce were offered in order to enrich the environment and improve the interaction between the animals and their handlers.

STUDY DESIGN

The animals were randomly assigned to one of two groups such that each group consisted of 1 male and 2 females.

The first group of animals (numbers 341M, 342F and 343F) were dosed according to the following regimen (dosages are in mg/kg):



IM Intramuscular
OG Oral gavage
IV Intravenous

* Oral doses were administered as [redacted] in the [redacted] and a further [redacted] in the [redacted]

\# [redacted] were administered as follows: [redacted] was administered by intravenous injection on Day [redacted]. On Days [redacted] inclusive, [redacted] was given orally

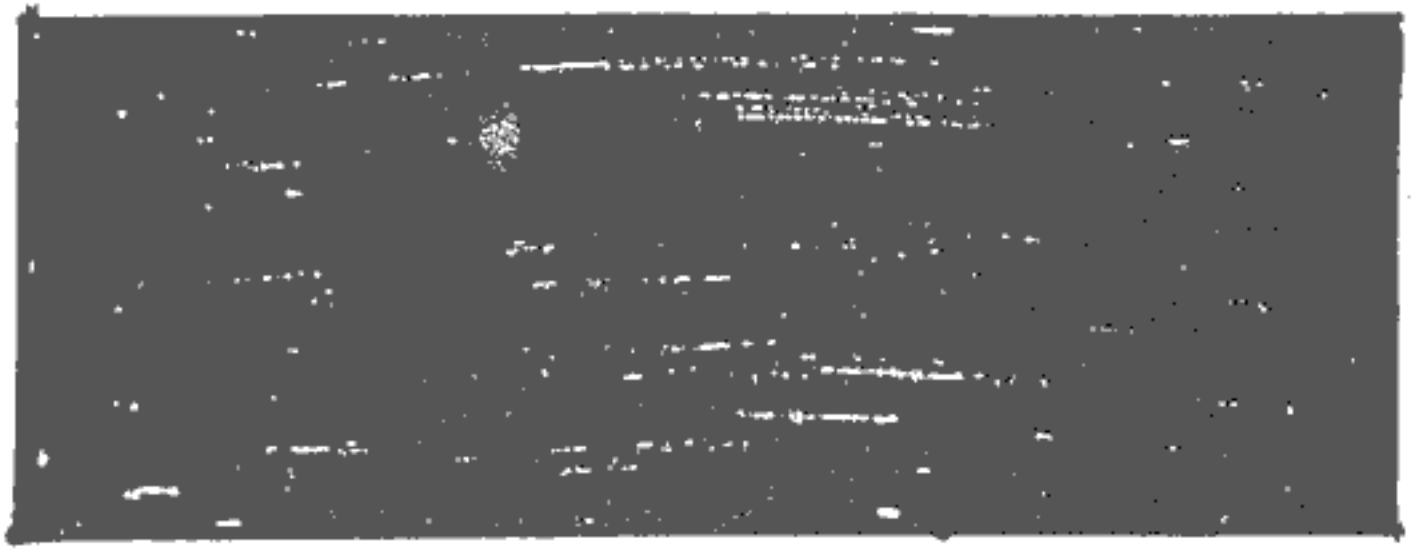
As the first group of animals did not develop thrombocytopenia, then the second group of animals (numbers 344M, 345F and 346F) was dosed according to the following schedule (doses expressed in mg/kg):

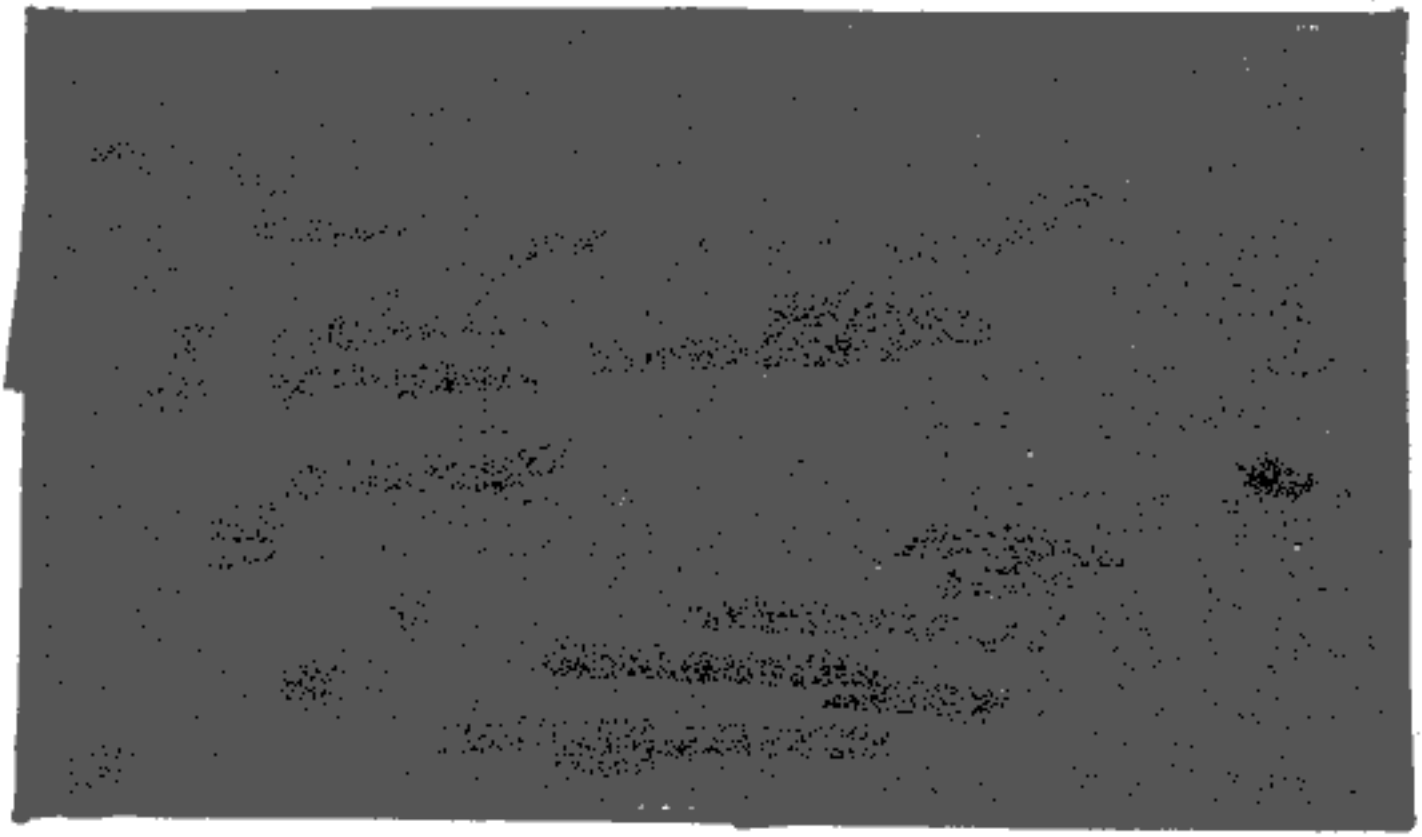
The animals were housed in the [redacted] Each cage was identified by a label and each label displayed the animal's individual identity number and study schedule number.

During the pre-dose period, each animal was allocated a permanent experimental number which was tattooed with India ink on the chest.

PREPARATION OF THE DOSE FORMULATIONS

Formulations were prepared for administration as follows:





ADMINISTRATION OF THE TEST SUBSTANCES

The animals were dosed at approximately the same time each morning and in the afternoon when applicable. Individual doses were adjusted according to the most recent bodyweight. The required quantity of each test solution was measured into a suitably graduated plastic syringe. For oral dosing, the test solutions were administered through a plastic catheter [redacted] inserted via the mouth into the stomach. The catheter was flushed through with tap water (approximately 10 ml).

For intravenous administration, the dose was administered through a venisystem butterfly set [redacted] inserted into a peripheral vein (cephalic or saphenous).

For intramuscular administration, the dose was administered through a 25G needle inserted into the biceps femoris muscle of the hindlimb.

Food was made available to the animals approximately one hour after the morning dose.

FORMULATION SAMPLING

With the exception o[redacted] the materials used in this study were licensed pharmaceutical products. Materials were used in accordance with the manufacturers instructions and formulation samples were not taken.

OBSERVATIONS

Dated and signed records of all activities relating to the day by day running and maintenance of the study within the animal unit as well as to the group observations and examinations outlined in this report, were recorded in the Study Day Book. In addition, observations relating to individual animals made throughout the day were recorded.

The following observations were made during the course of the study:

Clinical signs

All signs of ill health or reaction to treatment were recorded. Animals were checked regularly throughout the working day from 0900 to 1700 hours (including weekends).

Bodyweight

Bodyweight was recorded daily starting from Day -7. The animals were weighed in the morning prior to dosing or at a similar time during the pre-dose period.

Food consumption

The quantity of food (standard dry diet) left by individual animals and their spillage was recorded on a daily basis throughout the experimental period. From these data the quantities consumed were calculated.

Water consumption

The quantity of water consumed by individual animals was recorded daily from Day -7. The measurements were made by weighing of individual water bottles.

Body temperature

The body temperature (rectal) of each animal was measured daily, commencing on Day -7. Temperature was measured at approximately the same time each day.

LABORATORY INVESTIGATIONS

Laboratory investigations were performed according to the following schedule:

1. Haematology (Hb, PCV, RBC, WBC (Total and differential counts) and Platelets): Days -7, 2, 3, 4, 5, 6, 7 and 10.

2. Platelet aggregation Days -7 and 10.

3. Clotting tests (PT, APTT): Days -7, 5 and 10.

4. [redacted] blood level (0.5 ml whole blood in plain microtainer): blood despatched to the Sponsor for analysis: Days 3, 7 and 10. (Analysis and reporting of results is the responsibility of the Sponsor).

Blood samples were obtained from a femoral vein of each animal prior to dosing on the day of examination. The blood samples were placed into tubes containing the following anticoagulants:

EDTA anticoagulant..... for haematological investigations
Citrate anticoagulant..... for coagulation tests

The estimations performed on blood samples are listed below, together with an abbreviated title (for use in appendices), the methods and the units of measurement applicable at the time.

Haematology

	Units
The following estimations were performed using a Bayer-Technicon H1E haematology analyser:	
Packed cell volume (PCV)	%
Haemoglobin (Hb)	g/dl
Red cell count (RBC)	$\times 10^{12}/l$
Total white blood cell count (WBC Total)	$\times 10^{9}/l$

Units

Differential WBC count

Neutrophils	(N)	)	
Lymphocytes	(L)	)	
Eosinophils	(E)	)	
Basophils	(B)	)	$\times 10^9/l$
Monocytes	(M)	)	
Large unstained cells	(LUC)	)	

Cell morphology: the most common morphological changes (anisocytosis, micro/macrocytosis, variation in colour, hypo/hyperchromasia, left shift, atypical/blast cells) were recorded as follows:

-	=	no abnormalities detected
+	=	slight
++	=	moderate
+++	=	marked

Platelet count (Plt) $\times 10^9/l$

The following was performed using the appropriate methodology, as described below:

Prothrombin Time (PT) - Method of Quick, A.J. (1942) using an ACL 3000 Plus analyser and IL PT-Fibrinogen reagent s

Activated Partial Thromboplastin Time (APTT) - Method of Proctor, R.R., and Rapaport, S.I. (1961) using an ACL 3000 Plus analyser and IL APTT reagent s

Platelet aggregation - Method of Born, G.V.R., (1962), using ADP and Collagen as aggregating agents

TERMINAL STUDIES

On completion of 10 days' dosing (Day 11), all animals were killed.

Each animal was immobolised with [redacted] given by the intramuscular route. Bone marrow was obtained from each animal by sternal puncture. A smear was prepared and sent to the Sponsor for examination. Any examination and reporting of results was the responsibility of the Sponsor.

The animals were then killed by a lethal dose of [redacted] and discarded without further examination.

LOCATION OF STUDY RECORDS

All specimens, raw data and other documents generated at Huntingdon Life Sciences during the course of this study, together with a copy of the Final Report, will be lodged in the Huntingdon Life Sciences Archives, Huntingdon, England.

Such specimens and records will be retained for a minimum period of five years from the date of issue of the final report. At the end of the five year retention period the client will be contacted and advice sought on the future requirements. Under no circumstances will any item be discarded without the Sponsor's knowledge.

Any such material arising from investigations made by the Sponsor or other laboratory, the findings of which are included in the final report, are retained by the organisation conducting these investigations.

PROCEDURES

The procedures used during the study were those documented in the relevant Huntingdon Life Sciences Procedures Manual.

DEVIATIONS FROM PROTOCOL

Animals were not routinely fasted overnight prior to blood sampling. However, this is not considered to have had any effect on the parameters measured and therefore is not considered to be of any consequence.

Water consumption measurements were made gravimetrically rather than visually. Although this was not as described in the protocol, it is more accurate and therefore this deviation is not considered to be of any significance.

RESULTS

MORTALITY

There were no deaths.

CLINICAL SIGNS (Appendix 6)

Group 1

There was a gradual increase in the incidence of quietness and subdued behaviour as the study progressed. For the male, this began around Day 7, while for the females, quietness was first observed at Day 3. For the male, piloerection was seen from Day 8 and the animal was huddled with body tremors on Day 9. Salivation at dosing was seen on Day 10 only. Body tremors were also seen for female 343 on Days 9 and 10.

Group 2

Animal 344 male - The animal was quiet from Day 2, becoming subdued and huddled from Day 3. The animal vomited at around 1 hour after dosing on Day 4, and 6 minutes after dosing on Day 5. Salivation associated with dosing was seen on Days 5 and 6. From Day 6, the animal was paired with animal 345 female due to its condition and low body temperature (see below). The animal continued to be quiet, huddled and/or subdued until the end of the study. The animal passed liquid faeces from Day 8; piloerection was seen from Day 8.

Animal 345 female - The animal was quiet from Day 2, becoming subdued, with piloerection from Day 3. On Day 6, the animal was examined by a Veterinary Officer because it had become dehydrated and because of prolonged menstruation. 10 ml Haemocel and 30 ml Hartmanns fluid were administered intravenously; extra food supplements (including blackcurrant drink) were offered and the animal was paired with 344 male (as noted above). The animal continued to be quiet and huddled with occasional piloerection; on Day 10, liquid faeces were seen and the animal was subdued.

Animal 346 female - Piloerection, quietness and/or subdued behaviour were seen daily from Day 2. Huddled posture was noted on occasions from Day 7. From Day 6, the animal was offered extra blackcurrant drink because of slight dehydration and low temperature, and from Day 7, the animal was grouped together with animals 344 and 345. Liquid faeces were seen on Day 9, and the animal vomited at dosing on Day 10.

On veterinary advice, all Group 2 animals were given Emequell twice daily from Day 6.

APPENDIX 6

Individual clinical findings

Group: 1

Animal number: 341M

CLINICAL FINDINGS

The animal became increasingly quiet, subdued and huddled with piloerection during the last few days of the dosing period. Body tremors were noted on Day 9.

Incidental findings of a single incidence of salivation after dosing, loose faeces and rough coat were noted.

APPENDIX 6

(Individual clinical findings - continued)

Group: 1

Animal number: 342F

CLINICAL FINDINGS

The animal was noted to be quiet on Day 3, becoming increasingly subdued and huddled on the dosing period progressed.

The animal was noted to be menstrual on Day 10.

APPENDIX 6

(Individual clinical findings - continued)

Group: 1

Animal number: 343F

CLINICAL FINDINGS

The animal was quiet on Days 3 and 4 and was subdued and/or quiet daily from Day 7. Fine limb tremors were noted on Days 9 and 10.

The animal was first noted to be menstrual on Day 6 and this persisted until the end of the study.

APPENDIX 6

(Individual clinical findings - continued)

Group: 2

Animal number: 344M

CLINICAL FINDINGS

The animal was quiet from Day 2, becoming subdued and huddled from Day 3. The animal vomited at around 1 hour after the first dose on Day 4, and 6 minutes after the first dose on Day 5. Salivation associated with dosing was seen on Days 5 and 6. From Day 6, the animal was paired with animal 345 female due to its condition and low body temperature (see below). The animal continued to be quiet, huddled and/or subdued until the end of the study. The animal passed liquid faeces from Day 8; piloerection was seen from Day 8.

Emequell was given twice daily from Day 6 on veterinary advice.

Incidental finding of vocalising was noted.

APPENDIX 6

(Individual clinical findings - continued)

Group: 2

Animal number: 345F

CLINICAL FINDINGS

The animal was quiet from Day 2, becoming subdued, with piloerection from Day 3 and showing huddled posture from Day 4. On Day 6, the animal was examined by a Veterinary Officer because it had become dehydrated and because of prolonged menstruation. 10 ml Haemocel and 30 ml Hartmanns fluid were administered intravenously; extra food supplements (including blackcurrant drink) were offered and the animal was paired with 344 male. The animal continued to be quiet and huddled with occasional piloerection; on Day 10, liquid faeces were seen and the animal was subdued.

Emequell was given twice daily from Day 6 on veterinary advice.

The animal was noted to be menstrual from Day 2.

APPENDIX 6

(Individual clinical findings - continued)

Group: 2

Animal number: 346F

CLINICAL FINDINGS

Piloerection was seen from Day 2, quietness and/or subdued behaviour were seen from Day 3. Huddled posture was first noted on Day 7. From Day 6, the animal was offered extra blackcurrant drink because of slight dehydration and low temperature, and from Day 7, the animal was grouped together with animals 344 and 345. Liquid faeces were seen on Day 9, and the animal vomited approximately 20 minutes after the first dose on Day 6 and at dosing on Day 10.

Emequell was given twice daily from Day 6 on veterinary advice.

IAN001: HETEROTOPIC KIDNEY XENOTRANSPLANTATION IN CYNOLMOLGUS MONKEYS, WITH AND WITHOUT SPLENECTOMY: ITN4, ITN12, ITN13, ITN16, ITN18, ITN21, ITN26, IAN002,IAN004, IAN005, IAN008, IAN009, IAN010, IAN013, IAN017, IAN018, IAN020, and IAN022 are similar.

EXPERIMENTAL PROCEDURE

ANIMAL SUPPLY

Donor animals

Transgenic piglets were selected from litters produced by the Sponsor under Project Licence No. PPL [redacted]. Piglets supplied for the study were >21 days old and their weights in the range 6.5 - 9.0 kg.

Recipient animals

Captive-bred cynomolgus monkeys (*Macaca fascicularis*) were selected from shipments of animals bred at [redacted] Philippines. They were imported through a UK commercial supplier [redacted]. Their age at allocation to the study was 3 - 4¼ years and their weights in the range 2.7 to 3.8 kg.

The animals used in this study were selected from stock held on behalf of the Sponsor to undergo screening as suitable recipients. Based on the results of the prescreening investigations, animals were selected by the Sponsor for transplant (see. PRE-OPERATIVE INVESTIGATIONS). Whilst animals of either sex were selected, there was no specific requirement to maintain a balanced sex-ratio, as other selection criteria were more important. Only data relating to those animals that underwent transplant is presented in this report.

ANIMAL MANAGEMENT

Piglets

On the day of transplant, selected animals were delivered to Huntingdon Life Sciences by the Sponsor.

Cynomolgus monkeys

All animals were conditioned in England for at least 4 weeks before delivery to the Huntingdon Life Sciences. Documentation received from the supplier included details relating to quarantine dates, health screening and any treatment administered during the conditioning period. On arrival at Huntingdon Life Sciences they were examined by a Veterinary Officer and allocated a unique colony number, which was tattooed under the right arm. Intrapalpebral tuberculin tests were performed at intervals beginning soon after arrival. For transplanted animals, due to the frequency of planned laboratory investigations and by virtue of the fact that these animals were immunosuppressed, intrapalpebral tuberculin testing was stopped following transplant.

The animals were housed individually in cages specifically designed to house non-human primates in clean and secure conditions. The animals were housed in cages measuring 73 cm wide, 82 cm deep and 100 cm high. The cages were constructed of aluminium and electro-polished stainless steel, incorporating a squeeze-back system, food hopper, water bottle holder and a removable 2.5 x 2.5 cm grid floor. Under each cage was a urine collection tray. The cages were cleared of any faecal material or food residues each morning. The cages were changed at intervals of approximately 4 weeks. Water bottles were used for the supply of drinking water and were washed and refilled at least once daily.

If considered appropriate, upon completion of the first week following transplant, animals were paired up during the day with a non-transplanted animal. It is recognised that the pairing-up of animals may be beneficial to their continued post-operative recovery and long-term survival.

The rooms in which the animals were kept were, as far as practicable, isolated from external disturbances. The room temperature was maintained within the range 21 to 28°C, using heat exchangers connected to hot water supplied from oil-fuelled boilers. Relative humidity was maintained within the range 43 to 76%. The environment was governed by a computer controlled building management system which continuously monitored the temperature and humidity controls and the operational state of the air handling plant. Temperature and relative humidity were recorded using a Rototherm Recorder. Deviations in temperature and/or relative humidity outside the set limits (20 - 26°C, 45 - 70% RH) were generally due to the use of fan heaters as supplementary heat sources and when water was used to wash down cages and/or floors. Artificial lighting was used and was controlled to give 12 hours of light and 12 hours of dark per 24 hours. Air extraction was via a balanced system designed to give fifteen air changes per hour.

FOOD AND WATER

Cynomolgus monkeys were each offered 150 grams, of standard dry diet [redacted], daily each morning. In the morning before feeding, the residue of the previous day was removed and weighed. All animals were starved overnight prior to operation.

Water was available at all times. Vitamin C [redacted] and [redacted] (a vitamin B_{12} preparation, [redacted] were added to the drinking water on one day of each week.

There was no information available to the Study Director to indicate that any non-nutrient substance likely to influence the effect of the test substance could reasonably be expected to be present in the diet or the drinking water, both of which were routinely subjected to chemical analysis. Results of all the analyses were lodged in the Huntingdon Life Sciences Archives.

Wholemeal bread and fresh fruit or vegetable produce were offered in order to enrich the environment and improve the interaction between the animals and their handlers.

STUDY DESIGN

All animals were considered on an individual basis. A total of 17 animals underwent heterotopic renal xenograft transplant. The Sponsor was responsible for categorising the reasons why animals were sacrificed.

All animals that underwent transplant received immunosuppressive treatment with a combination of [redacted]

Details of donor-recipient pairings for transplants and the dates on which they were performed are listed in Appendix 1. All recipient animals were identified by their unique LS colony number.

The study was designed such that all animals initially followed a standard immunosuppressive protocol prior to and immediately following transplant. After a few days the immunosuppressive regime was then individually tailored for each animal being based on the results of laboratory investigations and blood drug levels.

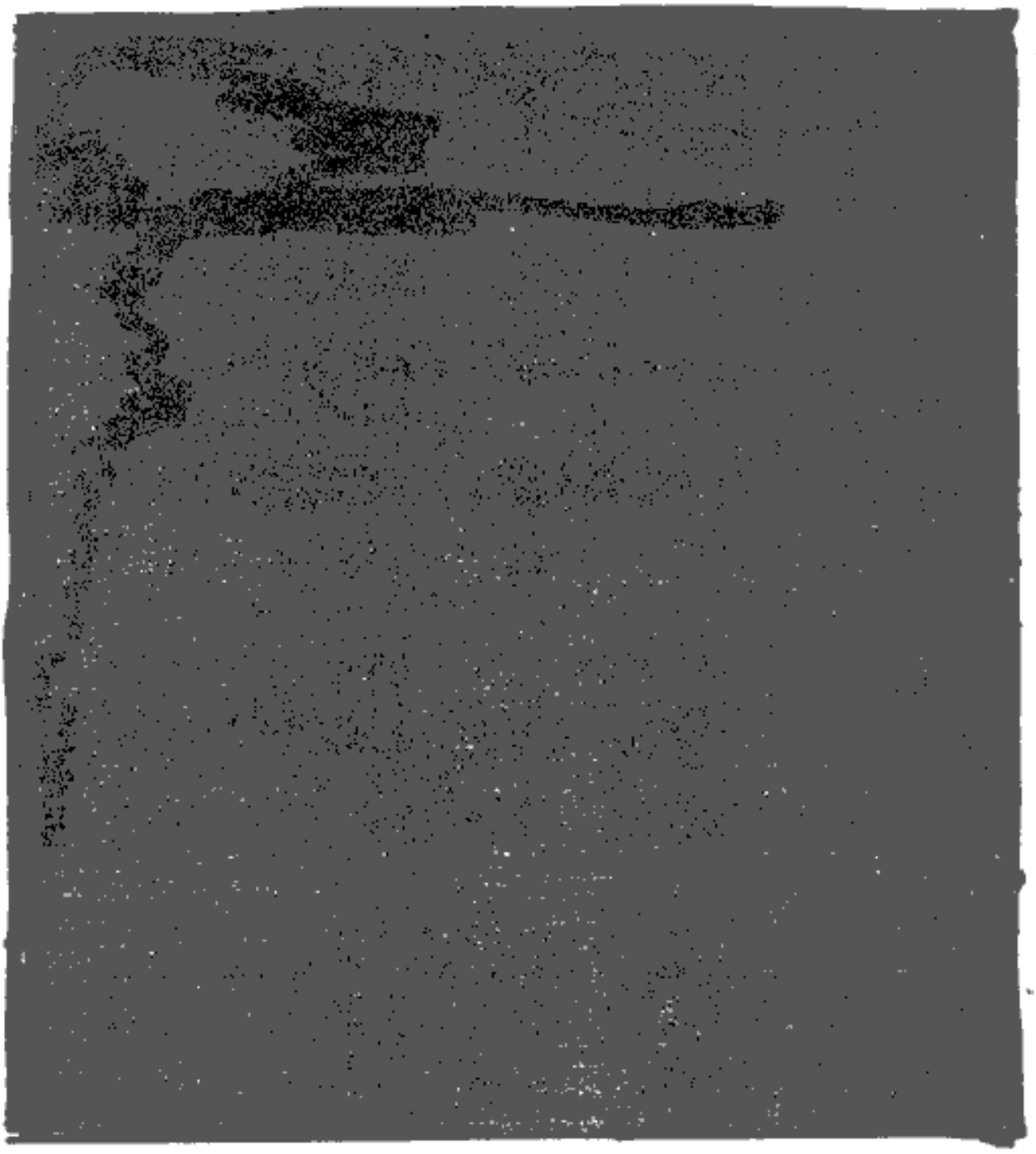
[redacted]

Details of the immunosuppressive regimes applied to individual animals are presented in Appendix 3. The initial dosing regimes are summarised as follows:

Transplant operations were performed on 1 or 2 recipient animals per day and were spread over a period of 6 weeks, dependent on the availability of suitable donor animals. The commencement of the study for these subgroups was therefore varied dependent on when the transplant was performed.

The animals were housed in th[redacted]

PREPARATION OF THE IMMUNOSUPPRESSANT TREATMENTS



FORMULATION SAMPLING

Details of batch usage were documented and records of daily preparation and administration of formulations were maintained. Formulation samples for analysis of achieved concentration and determination of homogeneity and stability were not taken.

ADMINISTRATION OF THE IMMUNOSUPPRESSANT TREATMENTS

The animals were dosed at approximately the same time each morning, late afternoon and evening when applicable. Individual doses were adjusted daily according to the most recent bodyweight. The required quantity of each test solution was measured into a suitably graduated plastic syringe.

For oral dosing the test solutions were administered through a plastic catheter [redacted] inserted *via* the mouth into the stomach. The catheter was flushed through with 10 ml of [redacted] (a high carbohydrate, low electrolyte, low fluid drink; [redacted]

For intravenous administration, the test solution was injected using a [redacted] infusion set inserted into the cephalic or saphenous vein.

For intramuscular administration, the test solution was injected through an appropriate gauge hypodermic needle. The animal was dosed in the thigh, the hair having been removed by clipping to facilitate administration and to observe any local reaction to the injection.

Intravenous administration of steroid on the day of transplant was carried out during surgery. The dose was administered through an indwelling cannula inserted into a peripheral vein (*ie* saphenous).

PRE-OPERATIVE INVESTIGATIONS

During the acclimatisation period, blood samples were obtained from potential recipient animals for investigations to enable the selection of the most compatible donor-recipient pairings. Blood samples were obtained for the following investigations.

Huntingdon Life Sciences

1. Pre-transplant haematology and biochemistry

Imutran Limited

1. Anti-pig antibody titres)
2. CH50) (9 ml into plain tubes)
3. Anti-∝GAL antibodies)
4. Endocrine assays) (1 ml EDTA)

Buccal swabs were also taken from each animal to determine the blood group.

Investigations carried out on donor animals were the responsibility of the Sponsor and, as such, have been documented and reported separately.

PRE-SURGERY TREATMENT

Commencing around 21 days prior to planned surgery, animals allocated for transplant commenced treatment with [redacted] in order to stimulate red cell production. Animals were dosed by subcutaneous injection twice weekly for 2 weeks at a dosage of [redacted] and at [redacted] twice weekly in the final week before transplant. On each dosing occasion, each animal also received [redacted] administered orally by gavage. Blood samples (0.3 ml EDTA and 0.7 ml Heparin) for haematology and biochemistry investigations were obtained prior to initiation of treatment and prior to transplantation. Weekly samples (0.3 ml EDTA) were also obtained for haematology investigations.

Any amendments to the dosing regimen or frequency of blood sampling for individual animals, as requested by the Sponsor, were documented in the study records. Any other treatments requested by the Sponsor were documented in the study records.

HETEROTOPIC RENAL TRANSPLANTATION

Renal transplantation in a primate weighing 2.6 - 3.8 kg is a procedure requiring microsurgical techniques. The donor and recipient animals were operated on simultaneously, thereby minimising the ischaemic time of the kidneys.

At the surgeon's discretion, various drug administrations were made during the surgical procedure, additional to those detailed in the protocol. Any such administrations were documented in the study records. Drugs given during the surgical procedure were normally administered intravenously unless stated otherwise in the protocol and/or study records.

Donor animals

During the preparation of the recipient, the donor animal was sedated with [redacted] administered by intramuscular injection at a dosage of [redacted] Anaesthesia was induced with [redacted] in a [redacted] mixture, delivered by a face mask. Initial induction of anaesthsia was by inhalation via a face mask and following transfer to the operating table, a tracheostomy was performed to allow endotracheal intubation and mechanical ventilation was commenced. The animal was maintained on a [redacted] mixture and [redacted] at a concentration of [redacted] A right sided neck incision was performed in order to obtain central venous access.

During the preparation of the recipient, the donor animal was sedated with [redacted] Initial induction of anaesthesia was by inhalation via a face mask and following transfer to the operating table, endotracheal intubation via tracheostomy was performed to allow mechanical ventilation. A right sided neck incision was performed in order to obtain central venous access.

The donor pig was placed supine on the operating table and aqueous [redacted] solution applied and sterile drapes placed in position, these being sutured to the skin. The abdomen was opened via a midline incision from slightly above the symphysis pubis to the mid-epigastrium. The wound was then held open with a self-retaining retractor.

Both kidneys were mobilised and removed. The right kidney was transplanted into the recipient. The left kidney was stored in preservation solution at ice temperature and was used if problems were encountered with perfusion of the right kidney.

The bowels were packed with a damp swab and retained in that position with a malleable lead retractor [redacted] was injected under the peritoneum around the hilum of each kidney in order to reduce the degree of spasm of the renal vessels during mobilisation of the kidney. The gonadal vessels were then dissected free of the ureter and controlled with a fine silicone sling. The ureters were mobilised with overlying peritoneum, controlled with slings, and then divided in the pelvis, as low as could be easily achieved. The distal ends of the ureters were ligated with 2:0 vicryl.

Stay sutures were placed in the perirenal tissue close to the upper and lower poles and used for holding the kidney thereafter; in this way, it was possible to avoid handling the kidney directly, which was important in preventing spasm in the renal vasculature. The peritoneum overlying the hilum of the kidney was carefully dissected and the renal artery and vein identified. The adrenal and gonadal vessels were ligated with 5:0 vicryl. A sling was placed around the renal vein which was retracted to enable the renal artery to be dissected to the aorta; 2:0 vicryl ligatures were then passed around the aorta immediately above and below the renal arteries. The final mobilisation of the kidney was then performed by dissecting posteriorly and haemostasis was carefully established.

When the dissection was complete, heparin was given intravenously at a dose of [redacted] this was allowed to circulate for at least two minutes. [redacted] at a dose of [redacted] and [redacted] at a dose of [redacted] was given. The aortic ligatures were then tied and the aorta transected so as to remove both renal arteries on a segment of aorta. Both renal veins were taken with a patch of inferior vena cava.

The kidneys were transferred to a bowl of cold Marshall's hypertonic citrate solution; this was maintained at ice temperature by the addition of blocks of frozen, sterile saline. Care was taken to avoid direct contact between the kidney and the frozen saline (which could cause local damage to the tissue) by enclosing the kidney in a swab. The kidneys were then separated by dividing the aorta longitudinally and each was perfused through the renal artery using a syringe and Wallace cannula; the perfusate consisted of [redacted] of heparin and [redacted] made up to [redacted] with Marshall's solution. Care was taken to avoid undue pressure by injecting very gently and also to avoid damage to the intima of the artery which might be caused by insertion of the cannula. If the surface of the kidney failed to blanch following perfusion of 20 ml of fluid, a further 20 - 40 ml of Marshall's solution was perfused. When well perfused and cold, the kidney was prepared for transplantation. The aorta was trimmed to form a small Carrel patch on the renal artery; the renal vein was prepared in a similar way. The kidney was then stored in the iced Marshall's solution until required for transplantation.

Recipient animals

The animal was fasted overnight prior to surgery. Whilst still in the animal unit, the animal was given an intramuscular unit, the animal was given an intramuscular injection of [redacted] and [redacted]. Once sedated, the animal was transferred to the operating suite. Cannulae were inserted into peripheral veins and an intravenous injection of [redacted] given. An intravenous injection of [redacted] was then given prior to insertion of an endotracheal tube, to assist intubation. [redacted] was subsequently administered by intravenous infusion during the surgical procedure, as required. [redacted] was administered by intravenous injection at a dosage of [redacted] The abdomen was then shaved.

An intravenous injection of [redacted] was given prior to insertion of an endotracheal tube, to assist intubation. [redacted] was subsequently administered during the surgical procedure by intravenous infusion as required. [redacted] was administered by intravenous injection at a dosage of [redacted] The abdomen was then shaved prior to transfer of the animal to the operating table.

The animal was transferred to the operating table where appropriate respiratory and electrocardiographic monitoring was established. Hartmann's solution was infused intravenously at a rate of [redacted] until the vascular anastomoses were completed, at which stage [redacted] was given intravenously and the infusion rate doubled. [redacted] was infused at an early stage of the procedure, before donor nephrectomy, in order to induce a rapid diuresis and minimise damage during transplantation. [redacted] was also infused at [redacted] at this stage.

The abdominal skin was then prepared with aqueous based [redacted] solution, and sterile drapes applied to expose the operative field. The abdomen was then opened via a midline incision from slightly above the symphysis pubis to the mid-epigastrium. The wound was held open with a self-retaining retractor.

The bowel was packed into the upper abdomen using a damp swab and malleable lead retractor. The peritoneum over the lower abdominal aorta was incised and the aorta mobilised from its bifurcation to the level of the inferior mesenteric artery. Silicone slings were passed around the aorta at each end of this dissection, taking care not to damage the lumbar arteries running posteriorly from the aorta. The inferior vena cava lying adjacent to this was then mobilised and two slings placed in a similar way. Heparin was then given at a dose of [redacted] and allowed to circulate for at least 2 minutes.

The aorta was elevated with the slings and a Cooley clamp applied from the right side; the clamp was then secured in the vertical position. (The intention of this manoeuvre was that the arteriotomy and subsequent anastomosis would lie slightly on the right side of the lower aorta, in order that, when the kidney was fixed in the right iliac fossa, the artery did not turn through a sharp angle and was, therefore, less likely to thrombose).

A transverse arteriotomy involving slightly less than half the circumference of the aorta was made with micro-scissors and the aorta irrigated with heparinised saline. The donor kidney was then removed from the ice and supported on the left side of the wound, using artery forceps as counterbalances attached to the stay sutures at the poles of the kidney. The kidney remained wrapped in a cold, soaked swab in order to keep it as cool as possible until it was revascularised. Double ended 8:0 ethylon sutures were placed at the upper and lower extremes of the arteriotomy; These sutures were then run down and tied, lowering the kidney into the wound in order to relieve any tension from the sutures. Working from each side of the anastomosis in turn, continuous sutures were inserted from both apices. These sutures were tied in the middle of each side.

The aortic clamp was left in place while the venous anastomosis was carried out. The inferior vena cava was elevated using the two slings and a second Cooley clamp applied in the same way as for the artery. A longitudinal venotomy was made using micro-scissors, this being approximately 50% longer than the apparent width of the vein. The renal vein was carefully orientated; the position of the adrenal and gonadal veins were helpful in this respect. A stay suture was placed at the lower extremity of the anastomosis; this was not tied until later. A double-ended 7:0 prolene suture was then placed at the upper extremity of the anastomosis and tied down. The posterior (medial) wall of the anastomosis was then consructed with a continuous suture from inside the vessel and then the anterior (lateral) wall from outside the vessel. The first suture was continued along the posterior wall, around the lower apex and half-way up the anterior wall; the other end of the double-ended suture was then used to complete the upper half of the anterior wall and the suture tied. At this stage the lower stay suture was tied.

Swabs were then placed around both anastomoses and the clamps gently removed from first the vein and then the artery. If oozing of blood from the anastomoses occurred, additional suturing was performed, in which case the clamp was briefly reapplied to enable this. When both anastomoses were haemostatic, [redacted] was applied to the vessels in an attempt to reduce spasm and increase renal blood flow. [redacted] was given intravenously at the time of revascularisation of the graft.

Two stay sutures were placed either side of the midline in the anterior wall of the bladder (which in the monkey is an intra-abdominal, rather than pelvic structure). The bladder was then opened anteriorly and the cystotomy held open with the two stay sutures laterally and a Babcock forceps retracting the superior end of the incision. This way, the posterior wall of the bladder was held relatively taut. A small incision was made in the mucosa in the lower part of the posterior wall and a submucosal tunnel created by passing a mosquito forceps in the submucosal plane in a cephalad direction for approximately 1 cm before passing through the detrusor muscle and out of the posterior wall of the bladder. The distal end of the ureter was then picked up with the mosquito forceps and pulled through the bladder wall.

Allowing sufficient length to prevent it from ever becoming taut, the ureter was partially divided by means of a transverse incision through slightly more than half its diameter and a small Watson-Cheyne probe passed. The ureter was then spatulated by means of an anterior longitudinal incision approximately 3 mm in length from the site of the transverse incision. In this way, the end of the ureter was splayed open in the form of a triangle. 6:0 vicryl sutures were then placed between each corner of the triangle and the cut edge of the bladder mucosa; these sutures were cut long, to act as stay sutures. Transection of the ureter was then completed and the distal remnant discarded. One more 6:0 vicryl suture was then placed in each gap between the three stay sutures and the stay sutures cut. The Watson-Cheyne probe was then passed into the ureter in order to check that the anastomosis was not stenosed. It was considered inadvisable to use more than six sutures for this anastomosis, even if mucosal apposition was incomplete, because of the risk of stenosis. The bladder was closed using two lengths of continuous 4:0 vicryl.

The transplanted kidney was then inspected once more and fixed in position. Several different techniques were used for this, one of which was to place the kidney in an extra-peritoneal pocket. This was created by lifting up the cut edge of the peritoneum close to the inferior vena cava and fashioning a pouch by blunt dissection in the right iliac fossa. The kidney was then passed posterior to the right gonadal vessels and ureter and located securely in the retroperitoneal space. However, the kidney, in some cases, did not lie well in this position and was then better placed in the optimum position and secured by suturing the fat and the peritoneum attached to the kidney to the peritoneum of the right or left iliac fossa. The appearance of the kidney was checked, before closing the abdomen, as perfusion of the graft may be very dependant upon position and a minor alteration in position at this stage may prevent subsequent thrombosis.

Both native kidneys were then removed from the recipient. The bowels were retracted and using a scalpel, an incision was made through the peritoneum overlying the kidney and the renal capsule. This incision was enlarged with scissors sufficiently to 'shell out' the kidney from its capsule. An artery forceps was placed across the renal pedicle as close to the renal hilum as possible in order to avoid the risk of damage to the inferior vena cava during mass ligation of the pedicle. The kidney was then excised and the pedicle doubly ligated with 2:0 vicryl. This intracapsular technique is very rapid, involves minimal dissection and is virtually bloodless. The spleen was also removed in selected animals.

All areas of dissection and, particularly, the anastomoses were then checked carefully for haemostasis and the donor kidney inspected to ensure that it appeared healthy and well perfused. The abdomen was then closed with a single layer of loop nylon to the linea alba, 2:0 vicryl to the subcutaneous tissues and the skin closed with subcuticular vicryl. Antiseptic spray was the applied to the wound.

Any notable deviations from these procedures were detailed in the study records.

POST-OPERATIVE MANAGEMENT

Recipient animals were closely monitored for the first 24 hours post-operation.

Animals received [redacted] which was administered intravenously twice daily for the first 5 days following transplantation.

Animals received heparin [redacted] during surgery and every eight hours for the first 24 hours following surgery. Heparin was administered by the subcutaneous route.

Animals received a single administration of [redacted] solution) and [redacted] on the day prior to transplant. From Day 1, up to three doses of [redacted] were given daily at the discretion of the attending veterinarian. Animals received a subcutaneous dosage of [redacted] Animals also received [redacted] if considered necessary.

Post-operative analgesia was provided by the use of [redacted] by intramuscular injection at a dosage level of [redacted] which was administered at the discretion of the attending veterinary surgeon.

Commencing from the day of transplant (Day 0) all animals recommenced treatment with [redacted] (see PRE-STUDY TREATMENT). Animals were dosed by subcutaneous injection daily at a dosage of [redacted] At the same time the animals also received [redacted] solution) given orally.

Other drugs were prescribed if considered appropriate. Details of individual drug administrations were recorded in the study records.

Following transplant, heat lamps were used to warm the animals until such time that their use was no longer required, as determined by the attending veterinarian.

The animals were observed at regular intervals during the working day and their condition reviewed.

Animals were given free access to drinking water and blackcurrant juice, which were continuously available. If voluntary fluid intake was considered insufficient, then this was supplemented by saline or other supportive fluids. Involuntary fluids were generally given intravenously if bowel function had not returned (which as usually within 24 - 48 hours after the operation), or given by oral gavage after recovery of bowel function. The type, route and amount of supportive therapy was determined by the attending veterinarian or duty surgeon.

[redacted] was given orally twice daily at a dosage of [redacted].

In the case of repeated or marked inappetance food and/or fluid (oral and/or intravenous) supplements were given at the discretion of the attending veterinary surgeon and/or Sponsor's monitoring scientist and were recorded in the study records.

POST-OPERATIVE OBSERVATIONS

Dated and signed records of all activities relating to the day by day running and maintenance of the study within the animal unit, as well as to the group observations and examinations outlined in this protocol, were recorded in the Study Day Book. In addition, observations relating to individual animals made throughout the day were recorded.

The following observations were made during the course of the study:

Mortality

The circumstances of any death were recorded in detail and a full *post mortem* examination performed as described later. Prior to death, observations and investigations listed below were carried out, if practicable.

Clinical signs

All signs of ill health or reaction to treatment were recorded. Animals were checked regularly throughout the working day from approximately 0900 to 1700 hours (including weekends and public holidays).

The animals were removed from their cages at regular intervals to assess their general condition (see POST-OPERATIVE INVESTIGATIONS).

Bodyweight

The bodyweight of all animals was recorded each week during the pre-dose period and daily during the post-operative period. The animals were weighed in the morning prior to dosing, or at a similar time during the pre-dosing period.

Food consumption

The quantity of food (standard dry diet) left by individual animals together with an estimate of the quantity spilled was recorded on a daily basis throughout the experimental period. From these data the quantities consumed were calculated.

Fluid consumption

Daily recording of fluid consumption/urine output commenced when individual animals had been identified and allocated for transplant. The quantity of water consumed by individual animals was recorded on a daily basis throughout the experimental period.

Urine output

The quantity of urine voided by individual animals was recorded on a daily basis throughout the experimental period commencing on the day prior to transplant (Day -1).

POST-OPERATIVE INVESTIGATIONS

Prior to the commencement of the study a specific post-operative schedule was prepared for each animal. Any subsequent deviations or changes to this schedule were documented in the study records.

Xenograft function and physical examination

Fluid consumption and urinary output were reviewed at regular intervals each day to determine how the transplanted kidney was functioning.

Based on these parameters animals were given fluid supplements (see **POST-OPERATIVE MANAGEMENT**).

When the animal was removed from its cage each morning and afternoon for dosing, a check of its general physical condition was also performed. At these occasions additional treatments (fluids, drugs, nutritional supplements etc.) were given to the animal as prescribed or directed by Huntingdon Life Science's veterinarians or the Sponsor's duty surgeon.

Laboratory investigations

Blood samples were obtained from each animal on the day prior to transplant (Day -1), the day of transplant and daily thereafter. The samples obtained and the investigations performed on them up to the first 15 days post-transplant were as shown overleaf:

Blood samples for endocrine assays, when requested by the Sponsor, were obtained on or shortly after arrival of the animals at Huntingdon Life Sciences, on one occasion prior to transplant (*ie* Day -1) approximately 7 days following transplantation and then approximately every 2 weeks. A 5 ml blood sample, for endocrine assay, was also taken prior to sacrifice.

Day	Volume	Investigation	Sample type
Day -1	0.5 ml	Anti-pig AB	Plain
	0.5 ml	Anti-alpha GAL	Plain
	0.5 ml	[redacted]	EDTA
Post [redacted] dosing:			
2 hours	0.5 ml	[redacted]	EDTA
12 hours	0.5 ml		EDTA
Day 0	1 ml	Held in immunol	Plain
Mondays	0.3 ml	Haematology	EDTA
	0.7 ml	Biochemistry	Heparin
	0.5 ml	Anti-pig AB	Plain
	0.5 ml	[redacted]	EDTA
	0.2 ml		EDTA
Tuesdays	0.3 ml	Haematology	EDTA
	0.5 ml	Anti-pig AB	Plain
	0.5 ml	[redacted]	EDTA
Wednesdays	0.3 ml	Haematology	EDTA
	0.7 ml	Biochemistry	Heparin
	0.5 ml	Anti-pig AB	Plain
	0.5 ml	[redacted]	EDTA
	0.2 ml		EDTA
Thursdays	0.3 ml	Haematology	EDTA
	0.5 ml	Anti-pig AB	Plain
	0.5 ml	[redacted]	EDTA
Fridays	0.3 ml	Haematology	EDTA
	0.7 ml	Biochemistry	Heparin
	0.5 ml	Anti-pig AB	Plain
	0.5 ml	[redacted]	EDTA
	0.2 ml		EDTA
Saturdays	0.3 ml	Haematology	EDTA
	0.5 ml	Anti-pig AB	Plain
	0.5 ml	[redacted]	EDTA
Sundays	0.3 ml	Haematology	EDTA
	0.5 ml	Anti-pig AB	Plain
	0.5 ml	[redacted]	EDTA

Thereafter, the frequency of the haematology investigations were reduced to 3 times per week (Mondays, Wednesdays and Fridays) and all other samples reduced at the Sponsors discretion, depending upon the general condition of the animal. Blood samples were obtained in the morning, prior to any dosing being performed. Biochemistry investigations were performed for the first 5 days post transplant and then at the intervals previously described.

Prior to transplant, a urine sample was collected from each animal for urinalysis investigations. Following transplant, urine samples were collected daily where possible. Urinalysis investigations were performed on Mondays, Wednesdays and Fridays. From the urine sample collected overnight, an aliquot of up to 20 ml was sent to the Sponsor.

The frequency of the laboratory investigations was increased or reduced for individual animals, dependent on their clinical condition, upon the recommendation of the attending Huntingdon Life Sciences veterinarian or Sponsor's Monitoring Scientist.

Additional parameters were investigated at the request of the Sponsor's Monitoring Scientist. The parameters were specified on the Huntingdon Life Sciences Clinical Pathology request form and were analysed according to standard Huntingdon methodology.

(a) **Laboratory investigations performed at Huntingdon Life Sciences**

Haematology	Units
300 µl into 0.5 ml EDTA tube. The following investigations were performed using a Bayer-Technicon H1E haematology analyser:	
Packed cell volume (PCV)	%
Haemoglobin (Hb)	g/dl
Red blood cell count (RBC)	$\times 10^{12}/l$
Total white cell count (WBC Total)	$\times 10^{9}/l$
Platelet count (Plts)	$\times 10^{9}/l$
Differential WBC count	
Neutrophils (N))	
Lymphocytes (L))	
Eosinophils (E))	$\times 10^{9}/l$
Basophils (B))	
Monocytes (M))	
Large unstained cells (LUC))	

Cell Morphology : the most common morphological changes (anisocytosis, micro/macrocytosis, variation in colour, hypo/hyperchromasia, left shift, atypical/blast cells) were recorded as follows:

- = No abnormalities detected
+ = slight
++ = moderate
+++ = marked

In the case of atypical/blast cells, or other abnormalities, confirmation or a written description from a blood film was made.

	Units
The following parameter was only investigated if considered necessary by the attending veterinarian or Sponsor's monitor, using the appropriate methodology as described below:	
Reticulocyte count (Retic) - method of Dacie, J. V. and Lewis, S. M. (Practical Haematology, 1966, 3rd edition, p. 28)	% (of red cells)

Biochemistry

700 µl into heparinised microtainer. The following parameters were analysed with a Hitachi 737 Clinical Chemistry analyser:

Urea	mg/dl
Creatinine (Creat)	mg/dl
Sodium (Na)	mEq/l
Potassium (K)	mEq/l
Calcium (Ca)	mEq/l
Inorganic Phosphorus (P)	mEq/l
Chloride (Cl)	mEq/l
Osmolality (Osmo) - using a Wescor vapour-pressure osmometer	mOsm/kg
Total Bilirubin (Bili-rubin)	mg/dl
Glutamic pyruvic transaminase (GPT), also known as 'Alanine aminotransferase' Reaction temperature 30°C	mU/ml
Glutamic-oxaloacetic transaminase (GOT), also known as 'Aspartate aminotransferase' Reaction temperature 30°C	mU/ml

The following parameters were analysed using a Roche Cobas Centrifugal analyser, using the appropriate BCL test kits:

Lactate dehydrogenase (LDH) Reaction temperature 30°C	mU/ml
Creatine phosphokinase (CPK) Reaction temperature 30°C	mU/ml
Amylase (Amyl-ase) Reaction temperature 37°C	mU/ml

	Units
*Uric acid Reaction temperature 30°C	mg/dl
Total protein	g/dl
Albumin (Alb)	g/dl
Globulin (Total Glob): by subtraction Total protein (g/dl) minus Albumin (g/dl)	g/dl

* These parameters were only investigated for individual animals if indicated by their clinical condition and as recommended by the Sponsor or attending Veterinarian.

Urinalysis

Volume (Vol)	ml
Specific gravity (SG) - by refractometry, compared to water with a value of 1000	
Urinary osmolality (Osmo) - using a Wescor vapour-pressure osmometer	mOsm/kg
The following parameters were analysed using a Roche Cobas Centrifugal analyser, using the appropriate BCL test kit:	
Urinary urea (U-Urea)	mg/vol
Urinary creatinine (U-Creat)	mg/vol
Uric acid (U-Uric acid)	mg/vol
The following parameters were analysed as described:	
Urinary Sodium (U-Na) - by flame photometry	mEq/vol
Urinary Potassium (U-K) - by flame photometry	mEq/vol
Urinary Chloride (U-Cl) - Roche Cobas Centrifugal analyser using BDH chloride reagent	mEq/vol

Units

The following were analysed as described:

The following parameter was analysed using a Beckman Protur HiSi Agarose gel electrophoresis kit:

Protein electrophoresis	mg/dl
Albumin (Alb)	mg/dl
Globulin (Glob)	mg/dl

The following parameter was analysed using a Roche Cobas Centrifugal analyser, using Randox Laboratories Ltd Total Protein (Urine) kit (Pyrogallol Red):

Total protein (Prot)	mg/dl

(b) **Blood samples for analyses by Sponsor or other laboratory**

Anti-pig antibody levels (Serum)

0.5 ml into a plain tube. Samples were analysed at [redacted]

Anti-alpha-Gal

0.5 ml into a plain tube. Samples obtained on Day -1 were analysed at [redacted]

Endocrine assays

1.0 ml into a 1 ml plain tube. Samples were analysed at [redacted]

0.2 ml into a 0.5 ml EDTA tube. Samples were analysed at [redacted]

[redacted] levels

0.5 ml into EDTA tube. The frequency of collection of blood samples for measurement of [redacted] levels was 0 hours (pre-treatment), 2 hours and 12 hours after administration of [redacted] and in the mornings thereafter, when requested by the Sponsor. Following collection of the blood samples, they were spun, the plasma was separated and stored deep frozen in cardice prior to despatch. The samples were sent to: [redacted] for analysis

TERMINAL STUDIES

The animals were maintained and dosed according to the immunosuppressive protocol unless sacrifice was required due to one of the following events occurring:

1. Evidence of renal failure. Signs of xenograft rejection were manifest by falling urine output, rising creatinine, listlessness and anorexia. These features are generally associated with a plasma creatinine in excess of 8 mg/dl (normal range 0.5 - 1.2 mg/dl).

2. Breakdown or marked infection of any wound site.

3. Systemic illness or marked deviation from its usual state of health.

4. Upon the advice of veterinary surgeons.

The Sponsor was contacted before any decision was taken to sacrifice an animal.

Pre-terminal blood sampling

Prior to sacrifice, as much blood as practicable was collected and divided appropriately into EDTA (5 ml) plain blood tubes (remainder). Following centrifugation, the serum was separated and deep frozen (in cardice) prior to despatch to the Sponsor for analysis.

Necropsy procedure

Each animal was immobilised wit[redacted] given by the intramuscular route. Bone marrow was obtained from each animal by sternal puncture and a smear prepared for subsequent staining and examination.

The animals were then killed by a lethal dose of [redacted] and then rapidly exsanguinated by incision of the carotid blood vessels.

Immediately after exsanguination the xenograft was carefully removed and weighed prior to taking any samples (see **Preservation of tissues**). The animal was then dissected and full macroscopic examination of tissues was performed, during which the following organs were dissected free of fat, removed and weighed, the paired organs being weighed separately:

adrenals	lungs	thyroids
brain	pancreas	uterus or prostate (with seminal vesicles)
heart	pituitary	testes (with epididymides) or ovaries
liver	thymus	

Preservation of tissues

Samples of the tissues and organs listed below were obtained from all animals and preserved for virus studies, pathology investigations and other investigations as detailed. For the various investigations tissue samples were preserved as follows:

Virus studies:	Samples were placed in cryovials and snap frozen in liquid nitrogen.
Pathology investigations:	Representative samples or the whole organ were preserved in neutral buffered formalin, with the exception of the eyes which were preserved in Davidson's fixative. Additional pieces of liver and kidney were also placed in formol calcium.
Other investigations:	As specified below.

Frozen samples were stored in cardice prior to despatch to the Sponsor on the next working day.

For individual animals other non-routine tissues taken at the discretion of the Sponsor's Monitoring Scientist were documented in the study records.

Tissue sampling requirements

Organ/tissue	Required for viral study (1)	Required for pathology investigations (2)	Required for other investigations
abdominal lining	√		
adrenals		√	
alimentary tract			
- oesophagus		√	
- stomach (body and antrum)	√	√	
- duodenum		√	
- jejunum		√	
- ileum	√	√	
- caecum		√	
- colon	√	√	
- rectum		√	
aorta			
- arch		√	
- abdominal		√	
brain (whole for)		√	
- cerebral cortex	√		
- thalamic nuclei			
- midbrain			
- medulla			
- cerebellum			
eye (with optic nerve)		√	
femur (with joint)		√	
gall bladder		√	
heart	√	√	
kidney (donor)	√	√	√ (3) (4)
liver	√	√	
lungs (with bronchi)	√	√	
lymph nodes			
- cervical		√	
- mesenteric	√	√	
- retroperitoneal	√	√	
macroscopic abnormalities		√	
mammary gland		√	

Organ/tissue	Required for viral study (1)	Required for pathology investigations (2)	Required for other investigations
ovaries	√	√	
pancreas	√	√	
pituitary		√	
prostate		√	
salivary gland (submandibular)		√	
sciatic nerve		√	
seminal vesicles		√	
skeletal muscle (quadriceps femoris)		√	
skin		√	
spinal cord (cervical, thoracic and lumbar regions)		√	
spleen	√	√	√ (3) (4)
sternum	√	√	√ (5)
testes (with epididymides)	√	√	
thymus		√	
thyroids (and parathyroids)		√	
tongue		√	
trachea		√	
urinary bladder		√	
uterus		√	
vagina		√	
vascular anastomoses	√	√	
5 ml whole blood (EDTA)			√ (6)
serum	√		

(1) ×6 cryovials for donor kidney; ×3 cryovials for all other samples
(2) All samples preserved in formalin, except for eyes which were preserved in Davidson's fixative. Additional pieces of liver and kidney were placed in formal calcium
(3) ×2 on cork disc
(4) ×2 cryovials
(5) bone marrow smear
(6) pre-terminal sample

ARCHIVING

All raw data, samples and specimens arising from the performance of this study will remain the property of the Sponsor.

All specimens arising from the work performed at Huntingdon Life Sciences and sent to the Sponsor or other Sponsor-nominated laboratory, are the responsibility of the Sponsor in respect of storage and archiving. Data and other records arising from any investigations performed on these specimens will be retained and archived by the Sponsor. All data and specimens relating to the donor animals are the responsibility of the Sponsor and will be retained and archived by them.

All other samples and specimens and all other raw data will be retained by Huntingdon Life Sciences in its archive for a period of five years from the date on which the Study Director signs the final report. After such time, the Sponsor will be contacted and his advice sought on the return, disposal or further retention of the materials. If requested, Huntingdon Life Sciences will continue to retain the materials subject to a reasonable fee being agreed with the Sponsor.

Huntingdon Life Sciences will retain the Quality Assurance records relevant to this study and a copy of the final report in its archive indefinately.

PROCEDURES

The procedures used during the study, except those associated with heterotopic renal transplantation, were documented in the relevant Huntingdon Life Sciences Procedures Manuals.

DEVIATIONS FROM PROTOCOL

Animals 206f and 212f sacrificed on Day 0 did not have *post mortems* performed as these animals were sacrificed in theatre and consequently organ weights were not recorded.

There were no other deviations from protocol other than those documented as File Notes or in the study records and which related to the clinical management of individual animals on a day-to-day basis.

APPENDIX 11

Individual clinical signs

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day, the signs are considered to be unrepresentative of the underlying condition of the animal.

2. Clinical signs are reported from the day following transplantation (Day 1).

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y204f	1	amp	Quiet but alert and sitting up, vomit in tray, no faeces
		m	Quiet but alert and sitting on perch, no faeces
	2	amp	Quiet but alert, huddled on perch, no faeces or urine passed overnight
		m	Quiet but alert, huddled on perch, no faeces or urine
	3	amp	Alert and active, sitting on perch, normal faeces
		m	Quiet and huddled on perch resting against ladder, drowsy, no faeces or urine
	4	am	Quiet and huddled on perch or lying on cage floor, normal faeces, sacrificed for humane reasons
Y206f	0	pm	Sacrificed in theatre following severe blood loss during operation, low Hb and unviable appearance of kidney
Y208m	1	am	Quiet and huddled on perch, eyelids partially closed, no faeces
		pm	Quiet and huddled, lying on floor, no faeces or urine
	2	am	Quiet but alert, lying on cage floor, appears uncomfortable, normal faeces
		pm	No movement, lying on cage floor, appears uncomfortable, no faeces
	3	am	Quiet but alert when stimulated, lying on cage floor
		pm	Quiet but alert and sitting on perch
	4	am	Quiet and huddled in corner of cage, reluctant to move
		pm	Quiet but alert, sitting on perch
	5	am	Left leg around cannulation site very swollen, bruised and necrotic. Not using leg at all. Sacrificed for humane reasons
Y214f	1	am	Bright and alert, occasionally active, sitting on perch, no faeces
		pm	Alert and active, no faeces or urine
	2	am	Alert and active , no faeces, vomited
		pm	Quiet, huddled on perch, no faeces
	3	am	Alert and active, moving round cage, slightly rough coat, normal faeces
		pm	Alert and active, no faeces
	4	am	Quiet but alert, no faeces
		pm	Quiet but alert, no faeces
	5	am	Quiet but alert, sitting on ladder, small amount of faeces passed
		pm	Quiet but alert, sitting on ladder, small amount of faeces passed
	6	am	Quiet but alert, sitting on perch, small amount of faeces passed
		pm	Quiet but alert, sitting on perch, small amount of faeces passed
	7	am	Quiet but alert, dark normal faeces
		pm	No comment recorded
	8	am	Quiet but alert, huddled on perch, pale, normal faeces
		pm	Quiet but alert, sitting on ladder, dark faeces
	9	am	Quiet but alert, huddled, leaning against ladder, no faeces
		pm	Quiet but alert, sitting on perch, no faeces
	10	am	Quiet but alert, huddled on perch, dark pelleted faeces
		pm	Quiet and huddled, leaning against ladder, alert when stimulated, no faeces
	11	am	Quiet and huddled but alert, active if approached, normal faeces
		pm	Quiet and huddled, sitting on perch or leaning against ladder, alert when stimulated, no faeces

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y214f (cont)	12	am	Alert but huddled, normal faeces
		pm	Quiet but alert, occasionally active
	13	am	Quiet but alert, sitting on perch, reluctant to move, dark pelleted faeces
		pm	Quiet but alert, no faeces
	14	am	Quiet, huddled across ladder, dark pelleted faeces
		pm	Quiet but alert, no faeces
	15	am	Quiet but alert, dark faeces
		pm	Quiet but alert, dark faeces
	16	am	Quiet, huddled on perch, normal faeces
		pm	Quiet, huddled on perch
	17	am	Quiet but alert
		pm	Quiet but alert, vomited
	18	am	Quiet but alert, standing on all fours on perch, loose faeces
		pm	Quiet but alert, sitting on perch, loose faeces
	19	am	Quiet but alert, loose/liquid faeces
		pm	Quiet, huddled and appears uncomfortable, no faeces
	20	am	Quiet but alert, dark loose faeces
		pm	Quiet, lying on ladder, no faeces
	21	am	Quiet, lying across ladder not moving, loose faeces
		pm	Quiet and huddled, lying across ladder, unusual posture, reluctant to move, no faeces. Sacrificed for humane reasons
Y216f	1	am	Alert but weak, slow movements, no faeces
		pm	Quiet but alert, sitting on ladder, no faeces
	2	am	Quiet but alert, sitting on perch, no faeces
		pm	Quiet but alert, no faeces
	3	am	Quiet but alert, sitting on perch, no faeces
		pm	Quiet but alert, sitting on ladder, no faeces
	4	am	Quiet but alert, sitting on perch, normal faeces
		pm	Quiet but alert, sitting on perch, wound slightly inflamed, normal faeces
	5	am	Quiet but alert, unusual posture, dark normal faeces
		pm	Quiet but alert, sitting in corner of cage on ladder, loose faeces
	6	am	Quiet but alert, normal faeces
		pm	No comment recorded
	7	am	Alert and active, slightly loose faeces
		pm	Alert and active, sitting on ladder, dark faeces
	8	am	Alert and active, no faeces
		pm	Alert and active, normal slightly dark faeces
	9	am	Quiet but alert and occasionally active, slightly loose/normal faeces
		pm	Quiet but alert, normal faeces
	10	am	Quiet but alert, slightly loose/normal faeces
		pm	Quiet but alert when stimulated, no faeces
	11	am	Quiet but alert, sitting on ladder, normal faeces
		pm	Quiet but alert, sitting on ladder
	12	am	Alert and active, occasionally quiet
		pm	Alert and active, occasionally quiet
	13	am	Quiet but alert, looking comfortable, loose faeces
		pm	Quiet but alert, no faeces

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y216f (cont)	14	am	Quiet but alert, loose faeces
		pm	Quiet but alert, normal faeces
	15	am	Alert and active
		pm	Alert and active
	16	am	Alert and aggressive, moving around cage
		pm	Alert and active
	17	am	Quiet but alert
		pm	Alert and active, slightly loose faeces
	18	am	Alert and active, normal faeces
		pm	Alert and active, vocalising, no faeces
	19	am	Alert and active, normal faeces
		pm	Alert and active
	20	am	Quiet but alert
		pm	Quiet but alert, sitting on perch, occasionally active
	21	am	Quiet but alert
		pm	Quiet but alert, active
	22	am	Quiet but alert
		pm	Quiet but alert, some movement around cage
	23	am	Quiet but alert, sitting on perch
		pm	Quiet but alert
	24	am	Alert and active, dark faeces
		pm	Quiet but alert, slightly active, sitting on perch, dark faeces
	25	am	Quiet but alert, dark faeces
		pm	Alert and active when stimulated, normal faeces
	26	am	Alert and vocalising, occasionally active
		pm	Alert and active
	27	am	Quiet but alert
		pm	Quiet but alert, occasionally active, no faeces
	28	am	Quiet but alert, dark faeces
		pm	Quiet but alert, active when stimulated, no faeces
	29	am	Alert and fairly active, normal faeces
		pm	Quiet but alert, dark faeces
	30	am	Alert and active, quiet at times, dark faeces
		pm	Alert and fairly active, normal faeces
	31	am	Alert and active, dark faeces
		pm	Quiet but alert, active when approached, no faeces
	32	am	Alert and active, dark faeces
		pm	Alert and active, dark faeces
	33	am	Alert and quite active, vocalising, normal faeces
		pm	Alert and active
	34	am	Quiet but alert, occasionally active
		pm	Quiet but alert, no faeces
	35	am	Quiet but alert, fairly active when approached, normal faeces
		pm	Quiet but alert, fairly active when approached
	36	am	Quiet but alert, occasionally active
		pm	Quiet but alert, no faeces
	37	am	Quiet but alert, dark faeces
		pm	Quiet but alert, dark faeces

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y216f (cont)	38	am	Quiet but alert, occasionally active, dark faeces
		pm	Quiet but alert, occasionally active, dark faeces
	39	am	Quiet but alert, standing in unusual posture, loose faeces
		pm	Quiet, slightly huddled, no faeces
	40	am	Alert and fairly active, sitting on perch, normal faeces
		pm	Quiet but alert, sitting on perch, no faeces
	41	am	Quiet but alert
		pm	Quiet but alert, lying on ladder, pale loose faeces
	42	am	Quiet and huddled on ladder, responds to external stimulation but reluctant to move, grey loose faeces
		pm	Quiet but alert, no faeces
	43	am	Quiet and huddled on ladder, vomited, grey faeces
		pm	Quiet and huddled, no faeces
	44	am	Quiet but alert, occasionally unsteady, high urine output overnight
		pm	Sacrificed for humane reasons
Y219m	1	am	Slow movements, no faeces
		pm	Lying down on cage floor, appears uncomfortable, alert when stimulated, no faeces
	2	am	Quiet but alert, sitting on cage floor, appears uncomfortable, normal faeces
		pm	Quiet but alert, sitting on perch.
	3	am	Quiet but alert, sitting on perch, no faeces
		pm	Quiet but alert, sitting on perch, no faeces
	4	am	Quiet but alert, sitting on perch or lying down, appears uncomfortable, normal faeces
		pm	Quiet but alert, sitting on perch.
	5	am	Quiet, crouched on cage floor or lying down.
		pm	Quiet but alert, sitting on perch
	6	am	Quiet, slightly huddled but alert
		pm	No comment recorded
	7	am	Quiet but alert, huddled on cage floor and leaning against perch
		pm	Quiet but alert, sitting on perch
	8	am	Quiet but alert, huddled on perch
		pm	Quiet but alert, sitting on ladder
	9	am	Quiet but alert, occasionally active, loose faeces, vomited
		pm	Quiet but alert, normal faeces
	10	am	Quiet and huddled on perch
		pm	Quiet but alert, sitting on ladder, loose/normal faeces, vomited
	11	am	Quiet but alert, sitting on perch and leaning against ladder, loose faeces
		pm	Quiet and huddled but alert, no faeces
	12	am	Quiet and huddled, became alert and active when stimulated, loose/liquid faeces
		pm	Quiet and huddled, became alert and active when stimulated, loose/liquid faeces, vomited twice
	13	am	Quiet and huddled, loose/liquid faeces, vomit
		pm	Quiet but alert, intermittently laying on cage floor, no faeces
	14	am	Quiet and huddled over ladder, loose faeces
		pm	Quiet but alert, no faeces

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y219m (cont)	15	am	Quiet but alert, normal faeces
		pm	Quiet but alert, lying huddled on perch, active when stimulated.
	16	am	Quiet but alert, huddled over ladder
		pm	Quiet and huddled over ladder, eyelids closed but alert if approached
	17	am	Quiet and huddled
		pm	Quiet but alert
	18	am	Quiet and huddled, alert when approached, vomited
		pm	Quiet, eyelids partially closed, no faeces
	19	am	Quiet, lying across ladder, alert when stimulated, loose faeces, vomited
		pm	Quiet, lying on ladder but moves when stimulated, no faeces
	20	am	Quiet and huddled, eyelids partially closed, no faeces
		pm	Quiet but alert, reluctant to move but showed slight activity, no faeces
	21	am	Quiet and lying on ladder, eyes partially closed, normal faeces
		pm	Alert and active, sitting on perch
	22	am	Quiet but alert, dark faeces
		pm	Alert, clinging to front of cage, no faeces
	23	am	Quiet but alert and sitting on perch, pelleted faeces, vomited
		pm	Quiet but alert, normal faeces
	24	am	Subdued and huddled, laying on ladder, appears asleep, reluctant to move when stimulated, loose faeces, vomited
		pm	Subdued and huddled lying against ladder, no reaction to external stimuli, very dehydrated, no faeces, vomited
	25	am	Quiet but alert, huddled on ladder, reacts to external stimulus, dark faeces, vomited
		pm	Quiet but alert reacts to external stimuli, no faeces
	26	am	Quiet and huddled but alert, dark faeces
		pm	Quiet but alert
	27	am	Quiet and huddled on perch, dark faeces
		pm	Quiet, sitting on ladder, normal faeces
	28	am	Quiet and huddled on ladder, dark faeces
		pm	Subdued and huddled on ladder, reluctant to move when stimulated, no faeces
	29	am	Quiet and huddled on perch, normal faeces, vomited
		pm	Quiet but alert.
	30	am	Subdued and huddled, lying on ladder, reluctant to move, abdomen and scrotum swollen and oedema around wound.
		Pm	Quiet and slightly subdued leaning against front of cage, slightly active when stimulated, vomited
	31	am	Subdued, huddled against ladder, slightly active when stimulated, oedematous, dark faeces
		pm	Very quiet and subdued, slumped over ladder, alert when stimulated, no faeces. Sacrificed for humane reasons.
Y209m	1	am	Alert and fairly active, no faeces
		pm	Alert and active, no faeces
	2	am	Alert and fairly active, occasionally lying down, straining to pass urine and faeces
		pm	Alert and fairly active, no faeces
	3	am	Alert and fairly active, normal faeces
		pm	Quiet but alert, active when approached, no faeces

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y209m (cont)	4	am	Alert but quiet, occasionally active, normal faeces
		pm	Alert and fairly active
	5	am	Quiet but alert, moves when stimulated, dark faeces
		pm	Quiet but alert
	6	am	Quiet but alert, dark loose faeces, vomited
		pm	Quiet but alert, sitting on ladder, normal faeces
	7	am	Quiet but alert, sitting on ladder
		pm	Quiet and huddled on cage floor, no faeces
	8	am	Quiet, spread across ladder in unusual posture or hunched on perch, straining when passing urine
		pm	Quiet and huddled in unusual posture between rungs of ladder , active if approached but otherwise reluctant to move, scratching at wound
	9	am	Quiet and huddled, eyelids partially closed, dark faeces
		pm	Quiet and huddled, disinterested in surroundings, alert when stimulated, no faeces
	10	am	Quiet but alert, sitting on perch, normal faeces
		pm	Quiet but alert, sitting on top of ladder, straining to pass urine and faeces, dark loose faeces
	11	am	Quiet but alert, sitting on top of ladder, dark faeces
		pm	Quiet but alert, loose/dark faeces
	12	am	Quiet but alert, subdued and hunched, unusual posture, straining to pass urine, loose/dark faeces
		pm	Quiet but alert, liquid faeces
	13	am	Quiet but alert, loose faeces
		pm	Quiet but alert and slightly active, loose faeces
	14	am	Quiet, unusual posture on ladder, loose faeces
		pm	Quiet and alert, sitting on ladder, normal faeces
	15	am	Quiet and huddled, sitting on cage floor or laying in a manner suggestive of colic, loose faeces
		pm	Quiet, no movement, looks uncomfortable, eyelids partially closed
	16	am	Quiet and huddled, loose faeces
		pm	Quiet and huddled over ladder, eyelids closed, loose faeces
	17	am	Quiet and huddled leaning against ladder, eyelids closed, dark liquid faeces
		pm	Quiet and huddled on perch, reluctant to move, very liquid faeces
	18	am	Quiet and subdued, huddled on perch, eyelids shut, vomit, liquid faeces
		pm	Collapsed, sacrificed for humane reasons
Y211m	1	am	Quiet and huddled, becomes active if stimulated, eyelids heavy, no faeces
		pm	Quiet and huddled, becomes active if stimulated, eyelids heavy, no faeces
	2	am	Quiet and huddled, sitting on perch, leaning against cage door, reluctant to move, eyelids heavy, no faeces
		pm	Quiet and huddled, sitting on perch, no faeces
	3	am	Quiet and huddled, leaning on drip catcher, normal faeces
		pm	Alert and active, moving around cage, no faeces
	4	am	Quiet and alert, sitting on perch leaning against ladder, slightly dark pelleted faeces
		pm	Quiet and huddled but alert, sitting on perch leaning against ladder, slightly dark pelleted faeces

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y211m (cont)	5	am	Subdued and huddled, reluctant to move, picking at wound, dark pelleted faeces
		pm	Quiet but alert, no faeces
	6	am	Quiet, huddled over ladder, dark pelleted faeces
		pm	Quiet, huddled over ladder, no faeces
	7	am	Quiet but alert, sitting on ladder, dark faeces
		pm	Quiet but alert, normal faeces
	8	am	Quiet but alert
		pm	Quiet but alert
	9	am	Quiet, huddled on perch
		pm	Quiet but alert
	10	am	Quiet but alert, sitting at top of ladder, slightly active.
		pm	Quiet but alert, sitting at top of ladder.
	11	am	Quiet but alert.
		pm	Quiet but alert, no faeces
	12	am	Quiet and huddled, normal faeces
		pm	Quiet and huddled
	13	am	Quiet but alert, normal faeces
		pm	Quiet but alert, slightly active, sitting on top of ladder.
	14	am	Quiet and huddled, sitting on top of ladder, dark faeces
		pm	Alert and fairly active, moving around cage, dark faeces
	15	am	Quiet and huddled on ladder, dark faeces
		pm	Alert and active, no faeces
	16	am	Quiet but alert, normal faeces
		pm	Quiet but alert
	17	am	Quiet but alert, sitting on top of ladder and occasionally active, dark faeces
		pm	Quiet but alert, slightly active, reacts to external stimulation, loose faeces
	18	am	Quiet but alert, reacts to external stimulation, dark faeces
		pm	Alert and active, moving around cage, dark faeces
	19	am	Alert and active, piloerection, vocalising, dark faeces
		pm	Alert and fairly active
	20	am	Quiet but alert, occasionally active, normal faeces
		pm	Quiet but alert, occasionally active, resting on perch, no faeces
	21	am	Quiet but alert, occasionally active, normal faeces
		pm	Subdued and huddled, leaning against ladder, reluctant to move when stimulated, no faeces
	22	am	Quiet but alert, becomes aggressive when approached, pelleted faeces
		pm	Quiet but alert, slightly active when stimulated, dark faeces, vomited
	23	am	Quiet but alert and sitting on perch, reluctant to move, slight swelling around both eyes, subcutaneous oedema on abdomen, dark faeces
		pm	Quiet but alert, sitting on ladder, dark pelleted faeces
	24	am	Quiet but alert, sitting on perch, slight swelling around both eyes, dark faeces
		pm	Quiet but alert, normal faeces
	25	am	Quiet but alert
		pm	Quiet but alert, dark faeces
	26	am	Quiet but alert, salivating, pelleted faeces
		pm	Quiet but alert, no faeces
	27	am	Quiet and huddled but alert, normal faeces
		pm	Quiet but alert, occasionally active

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y211m (cont)	28	am	Quiet but alert, dark faeces
		pm	Quiet but alert, dark faeces
	29	am	Quiet but alert, vocalising, appears puffy, normal faeces
		pm	Quiet, huddled over ladder
	30	am	Quiet but alert, no faeces
		pm	Quiet but alert, normal faeces
	31	am	Quiet and huddled, eyelids shut, reacts to external stimulation, dark faeces
		pm	Quiet and huddled, eyelids shut, reacts to external stimulation, no faeces
	32	am	Quiet but alert, normal faeces, vomited
		pm	Quiet and huddled, dark faeces
	33	am	Quiet and huddled, reluctant to move, normal faeces
		pm	Quiet and huddled on ladder
	34	am	Very quiet but alert, occasionally active, face puffy, dark pelleted faeces
		pm	Quiet and huddled, swelling around groin, normal faeces
	35	am	Quiet but alert, occasionally active, swelling around groin, dark faeces
		pm	Sacrificed for humane reasons
Y212f	0	pm	Sacrificed in theatre following excessive blood loss after transplant
Y220f	1	am	Quiet and huddled on ladder, normal faeces
		pm	Quiet but alert, no faeces
	2	am	Quiet and huddled, laying on ladder, becomes alert if stimulated, no faeces, vomited
		pm	Quiet and subdued, lying on ladder, reacts to external stimulation, dark faeces
	3	am	Quiet but alert, standing on ladder, reacts to external stimulation, dark faeces
		pm	Quiet but alert, sitting on ladder, reacts to external stimulation, dark faeces
	4	am	Quiet but alert, unusual posture, laying on ladder, scratching wound, normal faeces
		pm	Alert and fairly active
	5	am	Quiet, laying on ladder, reasonably alert, dark faeces, vomited
		pm	Quiet, laying on ladder
	6	am	Alert, occasionally active, pelleted dark faeces
		pm	Quiet but alert, reacts to external stimulation, dark faeces
	7	am	Alert and active, normal faeces, vomited
		pm	Quiet but alert, reluctant to move, dark faeces
	8	am	Quiet but alert, reluctant to move, dark faeces
		pm	Quiet but alert, normal faeces
	9	am	Alert, fairly active, no faeces
		pm	Alert, active when approached, no faeces
	10	am	Quiet but alert, fairly active, dark faeces
		pm	Alert, fairly active, dark faeces
	11	am	Quiet but alert, laying on ladder, dark pelleted faeces
		pm	Subdued, sitting on ladder, normal faeces
	12	am	Quiet but alert
		pm	Quiet and huddled but alert
	13	am	Quiet and huddled on perch, loose dark faeces
		pm	Alert and active

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y220f (cont)	14	am	Quiet but alert, occasionally active, making grunting sound when stressed, loose/liquid faeces
		pm	Quiet but alert, occasionally active, loose/liquid faeces
	15	am	Quiet but alert, no faeces
		pm	Quiet but alert, loose faeces
	16	am	Quiet and huddled but fairly alert, loose/liquid faeces
		pm	Quiet and huddled but fairly alert, no faeces
	17	am	Quiet and huddled but responds to external stimulation, loose faeces
		pm	Quiet but alert
	18	am	Alert and active, pale loose/liquid faeces
		pm	Quiet but alert, huddled on perch, no faeces
	19	am	Alert, fairly active, loose faeces
		pm	Quiet and huddled, no movement, no faeces
	20	am	Quiet, laying on ladder, dark pelleted and grey loose faeces
		pm	Quiet but alert, vomited
	21	am	Quiet but alert, sitting on ladder, loose faeces, vomited
		pm	Quiet but alert, no faeces
	22	am	Quiet and huddled on perch, occasionally active, responds to external stimulation, dark pelleted faeces
		pm	Quiet and huddled, loose/liquid faeces
	23	am	Quiet and huddled on ladder, responds to external stimulation, pale liquid faeces, vomited
		pm	Quiet and huddled on perch, no faeces
	24	am	Quiet but alert, sitting on perch, some loose/liquid
		pm	Quiet but alert, sitting on perch, loose/liquid faeces, vomited
	25	am	Quiet but alert, low urine output, vomited
		pm	Quiet and huddled on perch, low urine output, no faeces
	26	am	Quiet but alert, appears uncomfortable, very low urine output, loose faeces
		pm	Sacrificed for humane reasons
Y223f	1	am	Quiet, laying over ladder, no faeces
		pm	Quiet but alert, vomited
	2	am	Quiet but alert, sitting on ladder, showing interest in surroundings but reluctant to move, no faeces, vomited
		pm	Quiet but alert, laying on ladder, reacts to external stimuli, straining to pass urine, no faeces
	3	am	Quiet but alert, reacts to external stimulation, loose faeces
		pm	Quiet but alert, reacts to external stimulation, sitting on perch, no faeces
	4	am	Alert and active, no faeces
		pm	Alert and active, vomited
	5	am	Quiet but alert, occasionally active, normal faeces
		pm	Quiet, active at times, sitting on ladder, straining to pass urine, no faeces
	6	am	Quiet but alert, occasionally active, normal faeces
		pm	Quiet but alert, occasionally active.
	7	am	Alert, occasionally active
		pm	Quiet but alert, slightly active, dark faeces

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y223f (cont)	8	am	Quiet but very alert, occasionally active, dark faeces
		pm	Quiet but alert, occasionally active
	9	am	Alert and active, dark faeces
		pm	Quiet but alert, sitting on ladder, no faeces
	10	am	Alert and active, dark faeces
		pm	Alert and fairly active, dark faeces
	11	am	Alert and fairly active, vocalising, normal faeces
		pm	Active
	12	am	Quiet but alert
		pm	Quiet but alert
	13	am	Quiet but alert, dark faeces
		pm	Quiet but alert, dark faeces
	14	am	Alert and fairly active, normal faeces
		pm	Alert and fairly active, no faeces
	15	am	Alert and fairly active, dark faeces
		pm	Alert and fairly active, no faeces
	16	am	Quiet but alert, occasionally active, dark pelleted faeces
		pm	Quiet but alert, occasionally active, normal faeces
	17	am	Quiet but alert, occasionally active, dark pelleted faeces
		pm	Quiet but alert, sitting at top of ladder
	18	am	Alert and fairly active, normal faeces
		pm	Alert, occasionally active, no faeces, vomited
	19	am	Alert and fairly active, dark pelleted faeces
		pm	Quiet but alert, no faeces
	20	am	Quiet but alert, occasionally active, dark pelleted faeces
		pm	Quiet but alert, no faeces
	21	am	Quiet but alert, occasionally active, normal faeces
		pm	Quiet but alert, occasionally active, vomited
	22	am	Quiet but alert, reluctant to move, dark pelleted faeces
		pm	Alert, occasionally active or sitting quietly, dark pelleted faeces
	23	am	Quiet but alert, occasionally active, dark faeces
		pm	Quiet but alert, occasionally active, no faeces
	24	am	Quiet but alert, occasionally active, normal faeces
		pm	Quiet but alert and occasionally active, no faeces
	25	am	Quiet but alert and occasionally active, normal faeces
		pm	Alert and fairly active
	26	am	Quiet but alert, pelleted faeces
		pm	Quiet but alert, normal faeces
	27	am	Alert and active, pelleted faeces
		pm	Quiet but alert, sitting on ladder at front of cage, normal faeces
	28	am	Quiet but alert, vocalising, pelleted faeces
		pm	Quiet but alert, occasionally active, normal faeces
	29	am	Quiet but alert, active when approached, pelleted faeces
		pm	Pelleted faeces, vomited
	30	am	Quiet and huddled but alert, no movement, small amount of pelleted faeces
		pm	Quiet and huddled, pelleted faeces
	31	am	Quiet and huddled, alert but no movement, pelleted faeces
		pm	Quiet but alert, no faeces

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y223f (cont)	32	am	Quiet but alert, dark pelleted faeces
		pm	Quiet but alert
	33	am	Quiet but alert, pelleted faeces
		pm	Quiet but alert, occasionally active, normal faeces
	34	am	Alert, occasionally active, dark pelleted faeces
		pm	Alert, occasionally active, normal faeces
	35	am	Quiet and huddled
		pm	Quiet but alert
	36	am	Quiet and alert
		pm	Quiet but alert
	37	am	Quiet but alert, pelleted faeces
		pm	Quiet and huddled, no faeces
	38	am	Quiet, sitting on perch, eyelids closed, becomes alert when stimulated but reluctant to move, dark pelleted faeces, vomited
		pm	Quiet and huddled
	39	am	Quiet but alert, sitting on perch, reacts to external stimulation, lower urine output, pelleted faeces
		pm	Quiet but alert, hunched on perch, reacts to external stimulation, pelleted faeces
	40	am	Quiet and huddled, sitting on perch, appears sleepy, slight swelling above eyes, dark faeces, vomited
		pm	Subdued and huddled on ladder, appears asleep, slight swelling above eyes, reluctant to move when stimulated, urine output low, no faeces,
	41	am	Quiet and huddled on perch, appears drowsy, reluctant to move, urine output much increased, dark faeces, vomited
		pm	Quiet but alert, normal faeces
	42	am	Quiet and huddled on perch at back of cage, appears asleep
		pm	Quiet and huddled, sitting on ladder, appears sleepy, dark faeces
	43	am	Quiet but alert, sitting on perch, normal faeces
		pm	Quiet but alert, huddled on perch at back of cage
	44	am	Quiet but alert, sometimes active
		pm	Quiet but alert, huddled on perch
	45	am	Quiet but alert, sitting on cage floor
		pm	Alert and fairly active
	46	am	Quiet but alert, active when stimulated, pelleted faeces
		pm	Quiet, huddled on ladder, alert when stimulated, normal faeces
	47	am	Quiet and huddled, active when stimulated, good urine output
		pm	Quiet and huddled on ladder, no faeces
	48	am	Quiet and huddled but alert, low urine output, normal faeces
		pm	Alert, no faeces
	49	am	Quiet but alert, abdomen slightly distended, reasonable urine output, normal faeces
		pm	Alert and slightly active, dark faeces
	50	am	Quiet but alert, sitting on ladder, reasonable urine output, normal faeces
		pm	Quiet but alert, pelleted faeces
	51	am	Quiet and huddled at back of cage on perch, low urine output, pelleted faeces
		pm	Quiet and huddled, responds to external stimulation, normal faeces

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y223f (cont)	52	am	Subdued and huddled on perch, reluctant to move, vomited
		pm	Subdued and huddled on perch, reluctant to move, appears asleep, abdomen bloated, vomited
	53	am	Huddled but alert, oedematous
		pm	Sacrificed for humane reasons
Y222f	1	am	Quiet but alert, no faeces
		pm	Quiet but alert, no faeces
	2	am	Quiet but alert, sitting on cage floor, reluctant to move, no faeces
		pm	Quiet and huddled but alert, sitting on cage floor, normal faeces
	3	am	Very quiet but alert, leaning against front of cage not moving, no faeces
		pm	Very quiet but alert, leaning against front of cage not moving, no faeces. Sacrificed for humane reasons
Y226f	1	am	Quiet but alert, huddled on perch, no faeces
		pm	Quiet but alert
	2	am	Quiet but alert, sitting on perch, reluctant to move, few faeces
		pm	Very quiet and huddled, reluctant to move, no faeces
	3	am	Quiet but alert, sitting on perch, normal faeces
		pm	Quiet but alert and sitting on ladder, no faeces. Sacrificed for humane reasons
Y224f	1	am	Quiet but alert and sitting on perch, no faeces
		pm	Quiet but alert, no faeces
	2	am	Quiet but alert, bruising over wound, no faeces
		pm	Quiet but alert, no faeces
	3	am	Quiet but alert, sitting on perch, reacts to external stimulation, no faeces
		pm	Quiet but alert and sitting on perch, no faeces
	4	am	Quiet but alert, normal faeces
		pm	Quiet but alert, dark pelleted faeces
	5	am	Quiet but alert, occasionally active, normal faeces
		pm	Quiet but alert
	6	am	Quiet but alert, sitting on ladder, dark faeces
		pm	Quiet but alert, sitting on ladder, no faeces
	7	am	Quiet but alert, occasionally active, normal faeces
		pm	Quiet but alert, occasionally active
	8	am	Quiet but alert, dark faeces
		pm	Quiet but alert, dark faeces
	9	am	Quiet but alert, occasionally active, no faeces
		pm	Quiet and huddled, reluctant to move, no faeces
	10	am	Quiet and huddled but fairly alert, picking at wound, dark loose faeces
		pm	Quiet but alert, lip smacking when stimulated
	11	am	Quiet but alert, occasionally active, sitting on perch, no faeces
		pm	Quiet but alert, huddled on perch, no faeces
	12	am	Quiet but alert, occasionally active, no faeces
		pm	Quiet and huddled on perch, loose faeces
	13	am	Quiet but alert and fairly active, no faeces
		pm	Quiet but alert and fairly active, normal faeces

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y224f (cont)	14	am	Quiet but alert, threatening when looked at, loose faeces, vomited
		pm	Quiet and huddled on perch, no faeces
	15	am	Quiet and huddled on perch, responds to external stimulus but reluctant to move, no faeces, vomited
		pm	Sacrificed for humane reasons
Y200f	1	am	Quiet and huddled, laying or sitting on cage floor at rear, reluctant to move, becomes alert and vocal when stimulated , few faeces
		pm	Quiet but alert, sitting upright on cage floor, no faeces
	2	am	Quiet but alert, sitting on perch, face oedematous, no faeces
		pm	Quiet but alert, sitting on perch, no faeces
	3	am	Quiet but alert, no faeces
		pm	Quiet but alert, no faeces
	4	am	Quiet but alert, sitting on cage floor, wound swollen, no faeces, vomited
		pm	Quiet but alert, occasionally active, no faeces, vomited
	5	am	Quiet but quite alert, no faeces
		pm	Quiet but alert, normal faeces
	6	am	Alert and vocalising but sitting on cage floor, occasionally active.
		pm	Alert and active, no faeces
	7	am	Alert and fairly active, vocalising, aggressive when approached, piloerection around shoulders, normal faeces
		pm	Quiet, huddled over ladder or laying down, appears slightly subdued, dark faeces
	8	am	Quiet and huddled in corner of cage, dark faeces
		pm	Quiet and huddled in corner of cage, dark faeces, vomited
	9	am	Quiet but alert, reluctant to move, dark faeces
		pm	Quiet but alert, reluctant to move, no faeces
	10	am	Quiet but alert, normal faeces, vomited
		pm	Quiet and huddled.
	11	am	Quiet and huddled in corner of cage, reluctant to move, very withdrawn, no urine produced overnight, abdomen tense and distended with resultant dyspnoea, no faeces. Sacrificed for humane reasons
Y227m	1	am	Quiet and huddled or laying on floor, appears uncomfortable, alert if stimulated, occasionally showing an unusual posture, no faeces, vomited
		pm	Quiet and huddled, alert if stimulated, occasionally showing an unusual posture, no faeces, vomited
	2	am	Quiet and laying down on cage floor, no faeces
		pm	Placed in recovery box , appears more comfortable, still unresponsive to stimuli.
	3	am	Quiet and huddled, reacts to external stimuli, dark faeces
		pm	Quiet and huddled, reacts to external stimuli, no faeces
	4	am	Quiet but alert, sitting on perch with only occasional periods laying down, no faeces, vomited
		pm	Sacrificed for humane reasons

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y221f	1	am	Quiet but alert, resting on ladder, no faeces
		pm	Quiet but alert, no faeces
	2	am	Quiet but alert, resting on ladder, no faeces
		pm	Quiet but alert, resting on ladder, no faeces
	3	am	Alert and fairly active, no faeces
		pm	Alert and fairly active, dark pelleted faeces
	4	am	Alert and fairly active, dark pelleted faeces
		pm	Alert and active, dark pelleted faeces
	5	am	Alert and active, dark pelleted faeces
		pm	Quiet but alert, occasionally active, normal faeces
	6	am	Quiet but alert, no faeces
		pm	Quiet but alert, normal faeces
	7	am	Quiet but alert, dark pelleted faeces
		pm	Quiet but alert, no faeces
	8	am	Quiet but alert, moving in cage, normal faeces
		pm	Quiet but alert, occasionally active, dark pelleted faeces
	9	am	Quiet but alert, occasionally active, dark pelleted faeces
		pm	Quiet but alert, sitting on perch, normal faeces
	10	am	Quiet but alert, occasionally active, no faeces
		pm	Quiet but alert, occasionally active, no faeces
	11	am	Quiet but alert, laying on ladder, normal faeces
		pm	Quiet and huddled, alert when approached, no faeces
	12	am	Quiet but alert, occasionally active, dark pelleted faeces
		pm	Quiet but alert, occasionally active, normal faeces
	13	am	Quiet but alert, pelleted faeces
		pm	Alert and fairly active, normal faeces
	14	am	Alert and active, dark pelleted faeces
		pm	Quiet but alert, sitting on cage floor, normal faeces
	15	am	Unusual posture, looks uncomfortable, pelleted faeces
		pm	Alert, occasionally active, normal faeces
	16	am	Quiet but alert, sitting on perch, responds to external stimulation, dark faeces
		pm	Alert, normal faeces
	17	am	Alert and active, grooming partner.
		pm	Quiet but alert, pelleted faeces
	18	am	Quiet and huddled, being groomed by partner, normal faeces, vomited
		pm	Alert and active.
	19	am	Quiet and huddled but alert.
		pm	Quiet but alert, occasionally active
	20	am	Quiet but alert, sitting on cage floor, occasionally active, dark/loose faeces
		pm	Quiet but alert, occasionally active, loose faeces
	21	am	Quiet but alert, occasionally active, normal faeces
		pm	Alert, occasionally active
	22	am	Quiet but alert
		pm	Quiet but alert
	23	am	Quiet
		pm	Alert and active

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y221f (cont)	24	am	Alert and active, pelleted faeces
		pm	Quiet but alert, no faeces
	25	am	Quiet but alert, laying on ladder, moves when stimulated, dark pelleted faeces
		pm	Alert and active, normal faeces
	26	am	Alert and active, pelleted faeces
		pm	Alert and active, pelleted faeces
	27	am	Quiet and huddled, sitting on ladder, becomes alert when stimulated, dark pelleted faeces
		pm	Quiet but alert, sitting on ladder, occasionally active, normal faeces
	28	am	Quiet but alert, appears drowsy, sitting on ladder, becomes alert if approached, dark faeces
		pm	Quiet but alert, occasionally active, normal faeces
	29	am	Quiet but alert, occasionally active if stimulated
		pm	Quiet but alert, occasionally active if stimulated
	30	am	Quiet but alert, sitting on ladder, active if stimulated
		pm	Quiet but alert, grooming partner, dark loose faeces
	31	am	Quiet but alert, sitting on top of ladder, liquid faeces
		pm	Quiet but alert, sitting on perch, loose faeces
	32	am	Quiet but alert, sitting on ladder, loose faeces
		pm	Quiet but alert, normal faeces
	33	am	Quiet but alert, reacts to external stimulation, no faeces
		pm	Quiet but alert, no faeces
	34	am	Quiet, active when stimulated, sunken eyes, appears dehydrated, good urine output, pelleted faeces
		pm	Quiet and huddled on ladder, responds to external stimulation but reluctant to move, no faeces
	35	am	Quiet but alert, normal faeces
		pm	Alert
	36	am	Quiet but alert
		pm	Quiet but alert, occasionally active, dark faeces
	37	am	Quiet but alert, sitting on perch, normal faeces
		pm	Quiet but alert, on ladder
	38	am	Quiet and huddled on ladder, responds to external stimulation, low urine output, pelleted faeces, vomited
		pm	Quiet, sitting on floor in front of ladder, vomited
	39	am	Quiet but alert, huddled on cage floor, vocalising, normal faeces
		pm	Subdued and huddled, sunken eyes, vocalising, no faeces
	40	am	Quiet but alert, sitting on cage floor, thin and dehydrated
		pm	Quiet but alert
	41	am	Quiet but alert, occasionally active if stimulated, loose faeces
		pm	Sitting on perch, no faeces
	42	am	Quiet but alert, occasionally active if stimulated, normal faeces
		pm	Alert and active, vocalising, loose faeces
	43	am	Quiet and huddled but alert, no faeces
		pm	Quiet and lethargic, reduced urine output. Sacrificed for humane reasons.

APPENDIX 11

Individual clinical signs

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1).

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.	Observation
W435m	1 am	Loose faeces. Quiet, huddled. Very unsteady.
	pm	No urine passed. Distressed. Sacrificed.
W437m	1 am	Unsteady when moving. Quiet, huddled.
	pm	Sacrificed.
W338m	1 am	Quiet, huddled.
	pm	Quiet, subdued. Crouching on perch. Sacrificed.
W399m	1 am	Alert. No urine seen.
	pm	Very little movement. Quiet, huddled. Some urine (2-3ml) passed on handling.
	2 am	Alert and active. Approx. 20ml urine passed.
	pm	Quiet, huddled.
	3 am	Quiet, huddled.
	pm	Quiet, huddled but alert. No faeces
	4 am	Quiet but alert. No faeces
	pm	Quiet but alert. No faeces
	5 am	Quiet but alert. No faeces
	pm	Quiet but alert. No faeces
	6 am	Quiet but alert. Dark faeces.
	pm	Quiet but alert.
	7 am	Quiet but alert. Dark faeces.
	pm	Quiet but alert. Dark faeces.
	8 am	Quiet, huddled. Eyes swollen. Muzzle (left side) swollen. White frothy vomit in tray.
	pm	Quiet, huddled. Eyes swollen. Muzzle (left side) swollen.
	9 am	Quiet, huddled but very alert. Loose faeces.
	pm	Quiet, huddled.
	10 am	Quiet but alert. Operation site swollen.
	pm	Quiet but alert. Operation site swollen.
	11 am	Quiet but alert. Pale faeces. Operation site swollen.
	pm	Quiet but alert. Pale faeces. Operation site swollen.
	12 am	Quiet but alert.
	pm	Quiet but alert.
	13 am	Alert and active. Pale loose faeces.
	pm	Alert and active. Pale loose faeces.
	14 am	Quiet but alert. Pale loose faeces.
	pm	Alert and active. Loose faeces.
	15 am	Quiet but alert. Loose faeces.
	pm	Quiet but alert.
	16 am	Quiet but alert. Pale loose faeces.
	pm	Quiet but alert. Pale loose faeces.
	17 am	Quiet but alert. Pale loose faeces.
	pm	Quiet but alert.
	18 am	Quiet but alert.
	pm	Quiet but alert.
	19 am	Quiet but alert, huddled in hammock. Pale loose faeces.
	pm	Quiet but alert, huddled in hammock. Pale loose faeces.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.	Observation
W399m (cont'd)	20 am	Quiet but alert. Pale loose faeces.
	pm	Quiet, huddled.
	21 am	Quiet, huddled in hammock. Pelleted faeces.
	pm	Quiet, huddled in hammock. Scab on back of head.
	22 am	Quiet but alert. Pelleted faeces
	pm	Quiet but alert. Pelleted faeces
	23 am	Quiet but alert. Dark pelleted faeces.
	pm	Quiet but alert. Dark pelleted faeces.
	24 am	Quiet but alert. Dark pelleted faeces.
	pm	Quiet but alert. Dark pelleted faeces.
	25 am	Quiet but alert. Sitting in hammock.
	pm	Quiet but alert. Sitting in hammock.
	26 am	Quiet but alert.
	pm	Quiet but alert.
	27 am	Sacrificed.
W556f	1 am	Alert but quiet and active when disturbed. Red stained urine.
	pm	Alert, occasionally quiet and hunched. Periods of gentle activity.
	2 am	Quiet but alert.
	pm	Quiet but alert. Appears unsteady.
	3 am	Quiet but alert. Appears unsteady, legs appear weak.
	pm	Quiet but alert. Appears unsteady, legs appear weak.
	4 am	Alert. Very active. Appears agitated. Using legs better.
	pm	Alert and active. Vocalising.
	5 am	Alert and active. Appears agitated.
	pm	Quiet but alert.
	6 am	Alert. Bursts of activity.
	pm	Alert. Bursts of activity.
	7 am	Alert. Sitting in hammock.
	pm	Alert. Sitting in hammock.
	8 am	Quiet but alert. Pale loose faeces.
	pm	Quiet but alert. Pale loose faeces.
	9 am	Quiet but alert. Vomit in cage from previous nights dose of Calpol.
	pm	Quiet, huddled. Occasional vocalisation. No specific sign of pain on abdominal palpation. Normal faeces.
	10 am	Quiet, huddled but alert. Occasionally sits in hammock. Vomit in cage. Very dark urine.
	pm	Quiet but alert. Little activity.
	11 am	Quiet but alert.
	pm	Quiet but alert. Pale loose faeces.
	12 am	Quiet but alert. Normal faeces.
	pm	Quiet but alert. Vocal.
	13 am	Quiet but alert. Loose faeces.
	pm	Quiet but alert. Loose faeces.
	14 am	Quiet but alert. Normal faeces.
	pm	Quiet, huddled.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.	Observation
W556f (cont'd)	15 am	Quiet, huddled. Loose faeces.
	pm	Quiet, huddled.
	16 am	Very quiet, huddled. Oedematous swelling under eyelids. Normal faeces.
	pm	Sacrificed due to poor clinical condition.
W562f	1 am	Quiet. Reluctant to move.
	pm	Quiet but alert.
	2 am	Alert and active.
	pm	Alert and active.
	3 am	Alert and active.
	pm	Alert and active.
	4 am	Alert and active.
	pm	Alert and active.
	5 am	Alert and active. Slightly pale faeces.
	pm	Alert and active. Normal faeces.
	6 am	Alert and active.
	pm	Alert and active.
	7 am	Alert and active. Vomit in cage.
	pm	Alert and active.
	8 am	Alert and active. Pale faeces.
	pm	Alert and active. Pale faeces.
	9 am	Quiet but alert. Pale loose faeces.
	pm	Quiet but alert.
	10 am	Quiet but alert. Pale loose faeces. Blood in urine. Vomit in tray.
	pm	Quiet but alert.
	11 am	Quiet but alert. Blood in urine. Pale faeces.
	pm	Quiet but alert.
	12 am	Quiet but alert. Blood in urine.
	pm	Quiet but alert. Blood in urine.
	13 am	Quiet, huddled but alert. Blood in urine. Loose faeces.
	pm	Quiet, little movement. Unsteady when returned to cage. Loose faeces. Sacrificed.
W560f	1 am	Quiet and unsteady.
	pm	Quiet and huddled. Lying on cage floor. Eyes heavy lidded.
	2 am	Quiet and huddled. Loose faeces.
	pm	Sacrificed.
W548f	1 am	Still recovering from anaesthesia. Bloody urine passed.
	pm	Quiet but alert. Crouched on cage floor, reluctant to use legs.
	2 am	Quiet but alert. Reluctant to use legs.
	pm	Quiet but alert. Green vomit in cage .
	3 am	Quiet but alert. Legs seem slightly less swollen.
	pm	Quiet but alert. Reluctant to use legs.
	4 am	Quiet but alert. Using legs to move around more.
	pm	Quiet but alert. Using legs to move around.
	5 am	Quiet but alert.
	pm	Quiet but alert. Reluctant to move.
	6 am	Lying on cage floor. Very weak and unsteady when moving. Sacrificed .

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.	Observation
W552f	1 am	Very quiet and huddled. Still recovering from anaesthesia.
	pm	Quiet and huddled. Slow movements, minimal activity. No urine passed.
	2 am	Very quiet and huddled. No urine passed. Sitting on cage floor.
	pm	Sacrificed.
V337m	1 am	Quiet and huddled.
	pm	Quiet but alert, occasionally huddled. Some short periods of activity. Loose faeces.
	2 am	Quiet but alert, occasionally huddled. Loose faeces.
	pm	Appears asleep. Loose faeces.
	3 am	Alert and active. Loose faeces.
	pm	Quiet but alert.
	4 am	Quiet but alert. Loose faeces.
	pm	Quiet. Heavy lidded. Loose faeces.
	5 am	Quiet but alert. Loose faeces.
	pm	Quiet and huddled.
	6 am	Quiet and huddled, but alert.
	pm	Quiet and huddled, but alert.
	7 am	Very quiet and subdued. Occasional trembling. Appears unsteady.
	pm	Huddled. Unwilling to move. Collapsed state. Sacrificed.
T381m	1 am	Quiet, huddled. Unsteady movement.
	pm	Quiet, huddled. Heavy lidded. No movement.
	2 am	Quiet, huddled. No movement. No faeces
	pm	Appears asleep. No movement. No faeces
	3 am	Quiet but alert. No faeces
	pm	Quiet, huddled. No faeces
	4 am	Quiet, huddled. No faeces
	pm	Quiet, huddled. Minimal movement. No faeces
	5 am	Quiet, huddled. Loose dark faeces.
	pm	Quiet, huddled. Dark faeces.
	6 am	Quiet but alert. Shaking. Loose faeces
	pm	Quiet but alert. Shaking. Loose faeces
	7 am	Very quiet and subdued. Loose faeces.
	pm	Quiet, huddled. Loose faeces.
	8 am	Quiet. Little or no movement when stimulated. Loose faeces. Sacrificed.
T397m	1 am	Quiet but alert. Crouched appearance. No faeces.
	pm	Quiet and huddled. No faeces
	2 am	Quiet but alert, occasionally huddled.
	pm	Quiet but alert. Loose faeces.
	3 am	Quiet but alert.
	pm	Quiet but alert. Loose faeces.
	4 am	Quiet but alert. Occasionally huddled. Loose faeces.
	pm	Quiet but alert. Occasionally huddled. Loose faeces.
	5 am	Quiet but alert. Loose faeces.
	pm	Quiet but alert. Loose faeces.
	6 am	Quiet but alert. Loose faeces.
	pm	Quiet but alert. Loose faeces.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.	Observation
T397 (cont'd)	7 am	Quiet but alert. Occasionally huddled. Loose faeces. Some vomit seen in cage.
	pm	Quiet but alert.
	8 am	Quiet but alert. Normal faeces.
	pm	Quiet but alert.
	9 am	Quiet but alert.
	pm	Quiet but alert.
	10 am	Quiet, huddled. Vomit in cage.
	pm	Quiet but alert.
	11 am	Quiet but alert. Slightly huddled. Loose faeces.
	pm	Alert. .
	12 am	Quiet but alert. Vomit in cage.
	pm	Quiet but alert.
	13 am	Quiet. Normal faeces.
	pm	Quiet.
	14 am	Quiet but alert.
	pm	Quiet but alert.
	15 am	Quiet but alert. Occasionally huddled. Slight swelling around both eyes.
	pm	Quiet but alert. Occasionally huddled. Slight swelling around both eyes.
	16 am	Quiet but alert. Loose/liquid faeces.
	pm	Quiet but alert. Loose/liquid faeces.
	17 am	Quiet but alert. Occasionally huddled. Dark loose faeces.
	pm	Quiet but alert. Occasionally huddled.
	18 am	Quiet but alert. Occasionally huddled.
	pm	Quiet, huddled. Loose/normal faeces.
	19 am	Alert but reluctant to move. Loose faeces. Some vomit in tray.
	pm	Alert but reluctant to move. Loose faeces. Some vomit in tray.
	20 am	Quiet, huddled, reluctant to move. Vomit and liquid faeces in cage.
	pm	Inactive, huddled on cage floor/sitting posture.
	21 am	Quiet, huddled on perch, reluctant to move. No reaction to external stimuli, vacant appearance. Clear nasal discharge. Liquid faeces in cage.
	pm	Quiet, huddled on perch, reluctant to move. No reaction to external stimuli, vacant appearance. Clear nasal discharge. Liquid faeces in cage. Collapsed following administration of parenteral dosing. Some recovery, very quiet, sitting holding perch. Little interest in surroundings.
	22 am	Quiet and huddled. Reluctant to move. Constant grinding of teeth. Liquid faeces.
	pm	Quiet, huddled but alert. Liquid faeces.
	23 am	Quiet but alert. Liquid faeces.
	pm	Quiet, huddled but alert. Liquid faeces. Limited movement. Swelling in legs at dosing sites
	24 am	Quiet, huddled but alert. Liquid faeces. Clear nasal discharge.
	pm	Quiet, huddled, reluctant to move. No reaction to external stimuli. Loose/liquid faeces.
	25 am	Quiet, huddled but alert. Liquid faeces.
	pm	Quiet but alert. Liquid faeces.
	26 am	Quiet but alert. Liquid faeces.
	pm	Quiet but alert. Liquid faeces.
	27 am	Quiet and huddled on cage floor. Clear nasal discharge.
	pm	Quiet and huddled on cage floor. Clear nasal discharge.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.	Observation
T397m (cont'd)	28 am	Quiet, huddled but alert. Liquid faeces.
	pm	Quiet, huddled but alert. Liquid faeces.
	29 am	Quiet, huddled but alert. Liquid faeces.
	pm	Quiet, huddled but alert.
	30 am	Quiet but alert. Loose faeces. Vomit in cage.
	pm	Quiet but alert. Loose faeces. Vomit in cage.
	31 am	Quiet, huddled but alert. Liquid faeces.
	pm	Quiet but alert. Sitting on cage floor.
	32 am	Quiet, huddled but alert. Sitting on perch. Loose faeces.
	pm	Lying on cage floor.
	33 am	Lying down following blood sampling. Liquid faeces.
	pm	Quiet but alert, huddled. No faeces.
	34 am	Very quiet, huddled but alert. Swelling under both eyes. Loose faeces.
	pm	Very quiet, huddled but alert. Swelling under both eyes. Loose faeces.
	35 am	Quiet, huddled , alert at times. Appears weak. Seen to collapse. Sacrificed.
W151m	1 am	Very quiet. Eyes heavy lidded. Unusual crouched posture. No movement.
	pm	Quiet. Eyes heavy lidded. Unusual posture. No movement
	2 am	Quiet, huddled. Reluctant to move.
	pm	Quiet, huddled. Unusual posture. Eyes closed. No movement. Sacrificed.
V7m	1 am	Quiet, huddled but alert. Looking uncomfortable. Grinding teeth. Loose faeces. Bloody urine.
	pm	Quiet, huddled but alert. Looking uncomfortable. Grinding teeth. Loose faeces. Bloody urine.
	2 am	Quiet, huddled but alert. Loose faeces.
	pm	Quiet, huddled but alert. Loose faeces.
	3 am	Quiet, huddled but alert. Loose faeces.
	pm	Quiet but alert. Slightly less huddled. Loose faeces.
	4 am	Quiet but alert. Loose faeces.
	pm	Quiet and huddled. Reluctant to move. Periodically lying on cage floor. Appears uncomfortable. Occasional grinding of teeth.
	5 am	Quiet, sitting on cage floor, but alert. Loose faeces. Vomit in cage.
	pm	Quiet but alert.
	6 am	Quiet but alert. Loose faeces.
	pm	Quiet but alert. Loose faeces.
	7 am	Quiet but alert. Loose faeces.
	pm	Quiet but alert. Loose faeces.
	8 am	Quiet, huddled but alert.
	pm	Quiet, huddled. Little response to stimuli. Normal faeces seen.
	9 am	Quiet, huddled but alert.
	pm	Quiet, huddled but alert.
	10 am	Quiet, huddled but alert.
	pm	Crouched in corner of cage, salivating and retching. Later quiet but alert, no salivation.
	11 am	Quiet, huddled but alert.
	pm	Quiet but alert.
	12 am	Quiet but alert.
	pm	Quiet but alert.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.	Observation
V7m cont	13 am	Quiet but alert.
	pm	Quiet, huddled at back of cage.
	14 am	Quiet but alert.
	pm	Quiet but alert.
	15 am	Quiet but alert.
	pm	Quiet, huddled. Alert at times.
	16 am	Quiet but alert.
	pm	Quiet, unusual posture.
	17 am	Quiet but alert. Picking at left canine.
	pm	Quiet but alert.
	18 am	Quiet but alert. Pelleted faeces
	pm	Quiet but alert.
	19 am	Quiet but alert. Loose faeces.
	pm	Quiet, huddled but alert. No loose faeces
	20 am	Quiet but alert. Normal faeces.
	pm	Quiet but alert.
	21 am	Quiet but alert.
	pm	Sacrificed
T407m	1 am	Quiet, huddled but alert. Urine passed. No faeces
	pm	Quiet but alert. No faeces
	2 am	Quiet but alert. Dark faeces.
	pm	Quiet but alert.
	3 am	Quiet but alert. Normal faeces.
	pm	Quiet and huddled.
	4 am	Quiet but alert.
	pm	Quiet but alert.
	5 am	Quiet but alert.
	pm	Quiet, huddled but alert.
	6 am	Quiet and huddled. Loose faeces.
	pm	Appears cold. Extremely pale and very weak. Sacrificed.

APPENDIX 11

Individual clinical signs

Explanatory notes

Clinical signs are reported from the day following transplant (Day 1).

Only the first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day, the signs observed at these times were considered unrepresentative of the underlying condition of the animal.

APPENDIX 11

(Clinical signs -continued)

Animal No./sex	Day No.		Observation
W39m	1	am	Quiet.
		pm	Quiet, piloerection, reasonably bright.
	2	am	Quiet but alert, piloerection
		pm	Quiet but alert, no faeces passed, some blood stained urine passed.
	3	am	Quiet but alert, faeces passed, urine passed overnight.
		pm	Quiet but alert, no faeces seen.
	4	am	Quiet but alert, huddled, large amount of semi-digested vomit in tray, some loose faeces.
		pm	Quiet but alert.
	5	am	Very quiet but alert, huddled, small amount of loose faeces, semi-digested vomit.
		pm	Quiet but alert, huddled, small amount of loose faeces.
	6	am	Quiet but alert, huddled, small amount of loose faeces, eyes appear slightly sunken.
		pm	Alert, vomit in cage
	7	am	Quiet, huddled with head between legs, loose faeces, semi-digested vomit, very subdued, diarrhoeic.
		pm	Quiet, huddled, no faeces, much improved.
	8	am	Quiet, huddled and appears uncomfortable, occasionally alert, loose/liquid faeces.
		pm	Very quiet, huddled, sitting on cage floor, loose faeces. Sacrificed for humane reasons.
W144f	1	am	Quiet, huddled, reluctant to move, some urine passed overnight,no faeces passed.
		pm	Quiet, huddled, little response to stimuli, no urine/faeces passed.
	2	am	Very quiet, huddled on cage floor, unsteady, little/no movement, very small amount of urine/faeces passed
		pm	Sacrificed for humane reasons.
W47m	1	am	Quiet but alert, normal faeces, small amount of urine passed.
		pm	Quiet but alert, no faeces seen.
	2	am	Quiet but alert, normal faeces, urine slightly bloody.
		pm	Quiet but alert.
	3	am	Quiet but alert, loose pale faeces.
		pm	Quiet but alert, no faeces seen.
	4	am	Quiet but alert, loose pale faeces.
		pm	Quiet but alert, huddled, episodes of ventral recumbency,small amount of loose faeces.
	5	am	Quiet but alert, huddled, loose faeces passed, satisfactory urine output overnight.
		pm	Quiet but alert, huddled, no faeces seen, semi-digested vomit
	6	am	Quiet but alert, sitting on cage floor, piloerection, loose pale faeces, abdomen tender and swollen around wound.
		pm	Quiet but alert, occasionally huddled, no faeces seen.
	7	am	Quiet but alert, occasionally huddled, loose faeces.
		pm	Quiet and huddled, normal faeces.
	8	am	Quiet, very reluctant to move, very weak. Sacrificed for humane reasons.

APPENDIX 11

(Clinical signs - continued)

Animal No./sex	Day No.		Observation
V510f	1	am	Quiet but alert, normal faeces, small amount of urine passed.
		pm	Quiet but alert.
	2	am	Quiet and very huddled, pale, disinterested, some vomit, rectal temperature 37.5°C, some normal faeces.
		pm	Quiet and huddled, became alert when disturbed.
	3	am	Very quiet and huddled, sitting on cage floor but reasonably alert.
		pm	Quiet and sitting on cage floor, alert.
	4	am	Quiet and huddled, sitting on cage floor, became alert when disturbed, no faeces seen.
		pm	Quiet and huddled, sitting on cage floor, appears weak, semi-digested vomit.
	5	am	Quiet but alert, huddled, puffy around eyes, semi-digested vomit in tray , loose faeces passed, satisfactory urine output overnight.
		pm	Very quiet and huddled, periodically on cage floor. Later collapsed on cage floor. Sacrificed for humane reasons.
W43m	1	am	Quiet but alert, huddled, some normal faeces passed, 3ml of blood stained urine/vomit.
		pm	Quiet but alert, huddled, no faeces.
	2	am	Quiet but alert, huddled, no faeces.
		pm	Quiet but alert, huddled, no faeces and little urine passed.
	3	am	Quiet but alert, huddled, no faeces seen, semi-digested fruit vomit.
		pm	Quiet but alert, huddled, no faeces seen, semi-digested fruit vomit.
	4	am	Quiet but alert, clear mucous in loose/liquid faeces.
		pm	Quiet bit alert, no faeces seen.
	5	am	Quiet but alert, loose/liquid faeces, vomit in tray, urine output low.
		pm	
	6	am	Quiet, huddled, appears weak, small amount of loose faeces passed, very little urine passed overnight. Later collapsed.
		pm	Sacrificed for humane reasons.
V484f	1	am	Quiet, huddled, heavy lidded, no faeces.
		pm	Quiet but alert, occasionally huddled, no faeces.
	2	am	Quiet but alert, huddled, no faeces seen.
		pm	Quiet but alert, huddled, no faeces seen.
	3	am	Quiet, huddled on cage floor, no faeces seen, urine blood stained, appears tired and weak. Later collapsed on cage floor.
		pm	Sacrificed for humane reasons.

APPENDIX 12

Individual clinical signs

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1).

APPENDIX 12

(Clinical signs- continued)

Animal No./sex	Day No.		Observation
V812f	1	am	Quiet but alert, reluctant to move, siting on perch, salivating, piloerection, normal faeces, vomit in cage.
		pm	Quiet and huddled but alert, salivating, red stained vomit.
	2	am	Quiet, eyes closed, rough coat, no faeces seen.
		pm	Found collapsed on cage floor. Sacrificed for humane reasons.
W35m	1	am	Quiet but alert, sitting on perch, normal faeces.
		pm	Alert and active, no faeces seen.
	2	am	Very quiet and pale, continually laying on cage floor, faeces passed, swelling under abdominal wound, found collapsed. Sacrificed for humane reasons
W14f	1	am	Quiet but alert, urine and faeces passed, semi-digested vomit in tray.
		pm	Quiet but alert, vomit, grinding teeth.
	2	am	Quiet but alert, vomit in tray, loose faeces, good urine output.
		pm	Quiet but alert.
	3	am	Quiet but alert, normal faeces seen.
		pm	Quiet.
	4	am	Quiet but alert, good urine output.
		pm	Quiet but alert,
	5	am	Alert and active, very dark faeces, passing urine.
		pm	Quiet but alert, dark faeces.
	6	am	Alert, dark loose faeces.
		pm	Quiet but alert.
	7	am	Quiet but alert, dark loose faeces, semi-digested vomit.
		pm	Quiet but alert, huddled, sitting on cage floor, dark loose faeces.
	8	am	Found dead.
W27m	1	am	Quiet but alert, urine and faeces passed, semi-digested vomit in tray.
		pm	Quiet but alert, huddled on cage floor
	2	am	Very subdued but alert, cool peripheries, looks anaemic, normal faeces.
		pm	Quiet but alert, huddled.
	3	am	Very quiet with huddled/hunched posture, little interest shown to stimuli, piloerection, loose faeces.
		pm	Quiet.
	4	am	Quiet with huddled/hunched posture, good urine output, dark loose faeces, vomit in tray.
		pm	Quiet with huddled/hunched posture
	5	am	Very quiet and huddled, appears very sleepy, some swelling around both eyes, little response to stimuli, no faeces or urine passed.
		pm	Sacrificed for humane reasons.

APPENDIX 12

(Clinical signs- continued)

Animal No./sex	Day No.		Observation
X523m	1	am	Quiet, lying on perch, urine passed overnight, no faeces seen.
		pm	Quiet but bright, huddled on perch.
	2	am	Quiet but alert, huddled, no faeces seen.
		pm	Quiet but alert, huddled, no faeces seen.
	3	am	Quiet but alert, huddled, loose faeces, semi-digested vomit in tray, appears depressed.
		pm	Quiet and huddled, salivating.
	4	am	Quiet but alert, loose faeces, vomit in tray, listless, lying in cage and possibly exhibiting abdominal discomfort, frank haemorrhage from penis.
		pm	Quiet but alert, vomit.
	5	am	Quiet but alert, looking brighter, loose faeces.
		pm	Quiet but alert, some movement when observed, no faeces seen.
	6	am	Quiet but alert, vomit in tray, pale loose faeces (acute diarrhoea).
		pm	Very quiet and huddled, little response to stimuli, liquid faeces, abdomen tender.
	7	am	Quiet and huddled on cage floor, liquid/loose faeces
		pm	Sacrificed for humane reasons.
X527m	1	am	Quiet but alert, urine passed overnight, dark normal faeces.
		pm	Quiet but alert.
	2	am	Quiet but alert, huddled, dark faeces
		pm	Quiet but alert, huddled, observed vomiting, dark normal faeces.
	3	am	Quiet but alert, dark faeces.
		pm	Quiet and huddled, looking depressed, salivating, vomit and urine in tray.
	4	am	Quiet but alert, small amount of faeces, vomit in tray, listless, lying in cage and possibly exhibiting abdominal discomfort.
		pm	Quiet but alert, scratching wound.
	5	am	Quiet but alert, looking brighter, loose faeces, scratching wound.
		pm	Quiet but alert, reluctant to move, no faeces, vomit in cage.
	6	am	Quiet but alert, loose faeces (acute diarrhoea), vomit in tray.
		pm	Very quiet and huddled, liquid faeces, little response to stimuli, abdomen tender.
	7	am	Quiet but alert, scratching at side, loose faeces.
		pm	Sacrificed for humane reasons.
X529m	1	am	Alert, in lateral recumbent position on cage floor, exhibiting abdominal discomfort, reluctant to move but reacts to stimuli when handled, vomit in cage, normal faeces.
		pm	Alert but laying on cage floor, reluctant to move, sits up when stimulated, vomit in cage.
	2	am	Laying on cage floor. Sacrificed for humane reasons.
X522f	1	am	Quiet but alert, sitting on perch, loose/normal faeces.
		pm	Quiet but occasionally alert, huddled, sitting on perch.
	2	am	Quiet but alert.
		pm	Quiet and huddled, salivating profusely, liquid faeces.
	3	am	Quiet but alert, sitting on cage floor, occasionally huddled, no faeces seen.
		pm	No urine output since transplant. Sacrificed for humane reasons.

APPENDIX 11

Individual clinical signs

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1).

APPENDIX 11

(Individual clinical signs - continued)

Animal No./sex	Day No.		Observation
X525m	1	am	Lying on cage floor, reluctant to sit up. Faeces passed.
		pm	Subdued, sitting on perch, looking much brighter.
	2	am	Lying on cage floor, hunched, appears uncomfortable. No faeces seen
		pm	Lying on cage floor, appears uncomfortable.
	3	am	Alert and sitting on perch.
		pm	Quiet, lying on cage floor, unsteady whilst moving when disturbed.
	4	am	Quiet but alert.
		pm	Quiet but alert, seems less uncomfortable but still tense when handled.
	5	am	Quiet, lying on cage floor at times. Dark faeces, small vomit in tray.
		pm	Quiet, lying on cage floor at times. Dark faeces. No vomit seen.
	6	am	Quiet, lying on cage floor.
		pm	Quiet but alert, sitting or lying on cage floor, appears uncomfortable when abdomen palpated. Normal faeces.
	7	am	Quiet but alert, fairly active.
		pm	Quiet, lying on cage floor.
	8	am	Quiet and huddled, occasionally alert.
		pm	Very quiet, lying on cage floor, sits up when stimulated. Very little urine passed, no faeces seen.
	9	am	Quiet, lying on cage floor, reluctant to move, occasionally vocalising. Urine passed overnight.
		pm	Quiet, lying on cage floor, moves periodically, no faeces seen.
	10	am	Quiet and inactive, but alert. Occasional bursts of activity. Loose faeces.
		pm	Alert, sitting on perch, generally quiet and inactive.
	11	am	Quiet but alert. Normal faeces.
		pm	Alert and active.
	12	am	Quiet but alert.
		pm	Quiet and huddled, reluctant to move.
	13	am	Quiet but alert.
		pm	Quiet and huddled, reluctant to move.
	14	am	Alert, sitting on perch.
		pm	Alert and huddled on perch.
	15	am	Quiet but alert.
		pm	No comment made on animal condition.
	16	am	Alert, sitting on perch.
		pm	Alert, sitting on perch.
	17	am	Alert and active.
		pm	Alert and active.
	18	am	Quiet but alert.
		pm	Quiet but alert. Vocalising.
	19	am	Quiet but alert.
		pm	Alert and active, vocalising. No faeces seen.
	20	am	Alert and active. Normal faeces.
		pm	Alert and active.
	21	am	Quiet but alert, occasionally heavy lidded, becomes active when stimulated. Dark faeces.
		pm	Quiet but alert. Loose faeces.
	22	am	Quiet but alert. Loose faeces.
		pm	Quiet but alert, occasionally huddled on perch. No faeces seen.

APPENDIX 11

(Individual clinical signs - continued)

Animal No./sex	Day No.		Observation
X525m (contd)	23	am	Quiet but alert. Loose faeces.
		pm	Quiet but alert. No faeces seen.
	24	am	Quiet but alert. Loose faeces.
		pm	Quiet, heavy lidded, sitting on perch, becomes alert when stimulated. No faeces seen.
	25	am	Quiet but alert, sitting on perch. Liquid faeces.
		pm	Quiet and sitting huddled on perch or lying on cage floor, reluctant to move. Liquid faeces.
	26	am	Very subdued, lying huddled on cage floor, slow movements. Loose faeces, vomit in tray.
		pm	Very quiet but sitting on perch, subdued, eyes closed, reluctant to move. Appears very weak when stimulated. Liquid faeces.
	27	am	Very quiet and subdued, sitting on cage floor. Virtually anuric. Sacrificed for humane reasons
X531f	1	am	Quiet and huddled. Small amount of faeces passed.
		pm	Quiet, sitting on perch, very subdued, reluctant to move.
	2	am	Quiet but alert, huddled, appears uncomfortable. Dark faeces passed.
		pm	Quiet and huddled.
	3	am	Alert and active, sitting on perch. Heat lamp burn on back.
		pm	Quiet but alert, sitting on cage floor.
	4	am	Alert, sitting on perch.
		pm	Quiet but alert, sitting on perch.
	5	am	Quiet but alert. Dark faeces.
		pm	Quiet but alert, lying on cage floor. No faeces seen.
	6	am	Quiet but fairly active. Dark faeces.
		pm	Quiet and huddled, becomes alert when stimulated.
	7	am	Quiet and huddled in corner of cage.
		pm	Quiet, very subdued, appears asleep. Very little urine produced
	8	am	Quiet and huddled, occasionally alert. Normal faeces.
		pm	Very quiet, huddled, occasionally alert and shows some gentle activity, sitting on perch. Very little urine produced.
	9	am	Quiet and huddled, occasionally vocalising, reluctant to move. Urine passed overnight.
		pm	Very quiet, huddled and unsteady. Sacrificed for humane reasons.
X532f	1	am	Quiet and huddled, lying on cage floor, becomes active when stimulated. No faeces seen
		pm	Very quiet, continually lying on cage floor, appears uncomfortable. Minimal activity, moves when stimulated.
	2	am	Lying on cage floor, clinging to front of cage, appears uncomfortable. No faeces seen.
		pm	Quiet and huddled on perch clutching cage. Reluctant to move. No faeces seen.
	3	am	Quiet, generally improved, huddled at front of cage, heavy lidded, becomes alert when stimulated. Scratches on abdomen. No faeces seen.
		pm	Sitting on perch, holding onto cage, quiet and huddled but alert, weak when moving.

APPENDIX 11

(Individual clinical signs - continued)

Animal No./sex	Day No.		Observation
X532f (contd)	4	am	Quiet and huddled, alert when stimulated. Loose faeces. Vomit in tray.
		pm	Quiet and huddled, active if stimulated. Appears unsteady.
	5	am	Quiet and huddled but alert. Normal faeces.
		pm	Quiet and huddled, lying on cage floor. Dark faeces.
	6	am	Quiet and huddled.
		pm	Quiet and huddled.
	7	am	Quiet and huddled, intermittently lying on cage floor. Loose faeces.
		pm	Alert, sitting on perch. No faeces seen.
	8	am	Quiet and huddled, alert when stimulated. Loose faeces.
		pm	No comment made on animal condition.
	9	am	Alert, sitting on perch. Liquid faeces.
		pm	Alert, sitting on perch. Liquid faeces.
	10	am	Quiet but alert, sitting on perch. No faeces seen.
		pm	Quiet but alert, sitting on perch. No faeces seen.
	11	am	Quiet but alert, sitting on perch. No faeces seen.
		pm	Quiet but alert. No faeces seen.
	12	am	Alert, sitting on perch, vocalising. Liquid faeces.
		pm	Quiet and huddled, reluctant to move. No faeces seen.
	13	am	Quiet but alert. Loose faeces.
		pm	Alert and active. Loose faeces.
	14	am	Quiet but alert, sitting on cage floor, occasionally huddled. Pale liquid faeces.
		pm	Quiet but alert, sitting on perch. No faeces seen.
	15	am	Quiet but alert, sitting on cage floor. Loose faeces.
		pm	Quiet but alert, inactive on perch. No faeces seen.
	16	am	Quiet but alert, sitting on perch. No faeces seen.
		pm	Quiet but alert, sitting on perch. No faeces seen.
	17	am	Quiet but alert, standing on all fours. Grey coloured loose/liquid faeces.
		pm	Quiet but alert, sitting on perch. No faeces seen.
	18	am	Quiet but alert, sitting on perch. No faeces seen.
		pm	Quiet but alert, sitting on perch. No faeces seen.
	19	am	Quiet but alert, sitting on perch, vocalising. Grey coloured loose/liquid faeces.
		pm	Quiet but alert, slightly huddled. Pale loose faeces.
	20	am	Quiet but alert, reluctant to move. No faeces seen. Vomit in tray.
		pm	Quiet and inactive but alert, huddled on perch. No faeces seen.
	21	am	Quiet and huddled but alert. Vomit in tray. Liquid faeces.
		pm	Quiet and huddled but alert. Vomit in tray. Grey coloured liquid faeces.
	22	am	Quiet but alert, sitting at front of cage, reluctant to move. Pale loose/liquid faeces.
		pm	Quiet but alert, reluctant to move. Liquid faeces.
	23	am	Quiet but alert, sitting on perch. Liquid faeces.
		pm	Quiet but alert, sitting on perch. Liquid faeces containing blood. Blood in tray.
	24	am	Quiet, sitting in corner of cage, reluctant to move. Loose faeces, blood in cage.
		pm	Quiet, sitting in corner of cage, reluctant to move. Grey coloured liquid faeces. Blood in cage.
	25	am	Slightly subdued, sitting on perch. Grey/white liquid faeces. No blood seen in faeces.
		pm	Lying on cage floor or sitting huddled on perch, subdued and inactive. Grey/white liquid faeces.
	26	am	Very quiet and subdued, reluctant to move, raises head when stimulated. Pale liquid faeces, vomit in tray.
		pm	Sacrificed for humane reasons.

APPENDIX 11

(Individual clinical signs - continued)

Animal No./sex	Day No.		Observation
X537f	1	am	Quiet and huddled, lying on cage floor. Appears uncomfortable.
		pm	Continually lying on cage floor. Will move when disturbed.
	2	am	Quiet and huddled on cage floor, occasionally sitting up. No faeces seen. Vomit in tray.
		pm	Quiet and huddled in corner of cage, reluctant to move, appears uncomfortable.
	3	am	Quiet but alert, sitting on perch, reluctant to move, occasionally huddled and heavy lidded. Appeared uncomfortable. Abdomen scratched. Dark faeces.
		pm	Small vomit post dosing.
	4	am	Showing signs of discomfort, intermittently lying on cage floor, quiet but alert. Abdomen seems enlarged. Loose faeces. Vomit in tray.
		pm	Quiet and huddled in corner of cage, little or no movement, alert only if stimulated.
	5	am	Lying on cage floor, very poor condition. Vomit in tray. Sacrificed for humane reasons.
X528f	1	am	Lying on cage floor, becomes alert and stands up when stimulated. No faeces seen. Vomit in tray.
		pm	Lying on cage floor, becomes alert and stands up when stimulated. No faeces seen.
	2	am	Quiet but alert, sitting on perch. No faeces seen.
		pm	Quiet but alert, sitting on cage floor, moves when stimulated. No faeces seen.
	3	am	Quiet but alert, lying on cage floor or standing on all fours. No faeces seen. Vomit in tray.
		pm	Alert.
	4	am	Quiet but alert, sitting upright or lying on cage floor, moves when stimulated. No faeces seen. Vomit in tray.
		pm	Quiet, lying on cage floor, becomes alert and sits up when stimulated. Dark faeces.
	5	am	Quiet and alert, sitting upright. Normal faeces.
		pm	Lying or sitting on cage floor, alert but reluctant to move. No faeces seen.
	6	am	Lying on cage floor, becomes more alert when observed. No faeces seen
		pm	Vomited during dosing, sitting on perch. Loose faeces. Vomit in tray.
	7	am	Quiet but alert, sitting on perch. Loose/liquid faeces.
		pm	Quiet but alert, sitting on perch, occasionally huddled. Loose/liquid faeces.
	8	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert, sitting on perch.
	9	am	Quiet but alert, sitting on perch. Liquid faeces.
		pm	Quiet and huddled on perch, reluctant to move. No faeces seen.
	10	am	Poor condition, bruising and skin petechiae, subdued and huddled on perch, reluctant to move. Grey/white loose faeces.
		pm	Subdued, lying on cage floor, bruising on face and arms. Later weak, lying on cage floor, subdued, inactive, in crouched position showing limited response to touch.
	11	am	Very quiet and subdued, sitting on cage floor in huddled posture, occasionally lying down, sits up when stimulated. Pale liquid faeces. Vomit in tray. Sacrificed for humane reasons.

APPENDIX 11

(Individual clinical signs - continued)

Animal No./sex	Day No.		Observation
X524f	1	am	Lying on cage floor but showing good response on observation. Appears weak. No faeces passed.
		pm	Very subdued, lying on cage floor, no reaction to stimulation, eyes closed. No faeces seen.
	2	am	Lying on cage floor or sitting on perch. Salivated post dosing. Faeces seen
		pm	Sitting on cage floor.
	3	am	Looking brighter, sitting on cage floor leaning on perch. Appears weak. Very little urine production.
		pm	Quiet, huddled on perch. No faeces seen.
	4	am	Quiet, sitting huddled on perch, appears weak. Very dark liquid faeces.
		pm	Quiet, huddled on perch with head held in its hands. No faeces seen. Sacrificed for humane reasons.
X536f	1	am	Sitting in corner of cage, trying to sleep. No activity. No faeces seen.
		pm	Subdued, sitting on perch, slightly unbalanced. Later alert with occasional activity. No faeces seen.
	2	am	Quiet and huddled but alert. Clear mucus in faeces. Salivation post dosing.
		pm	Quiet, sitting on cage floor.
	3	am	Quiet but alert, sitting on cage floor.
		pm	Quiet but alert, huddled on perch. Loose faeces.
	4	am	Quiet and huddled, looking very weak. Loose faeces.
		pm	Quiet and huddled on perch, looking very weak with head in hands. No faeces seen. Vomiting profusely.
	5	am	Quiet and huddled, heavy lidded, appears weak when handled, reluctant to move. Loose faeces.
		pm	Sacrificed for humane reasons.

APPENDIX 11

Individual clinical signs

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1) where applicable.

APPENDIX 11

(Individual clinical signs - continued)

Animal No./sex	Day No.		Observation
X534f	0	pm	Very subdued, lying on cage floor, not responding to stimuli. Sacrificed for humane reasons.
X541f	1	am	Sitting on perch but unsteady, alert but weak, no urine or faeces seen.
		pm	Quiet but alert, sitting on perch, abdomen appears swollen, small amount of normal faeces.
	2	am	Alert but occasionally quiet, abdomen less swollen, passing clear urine.
		pm	Quiet but alert, occasionally huddled, looked discomforted.
	3	am	Quiet but alert, becomes active when observed, occasionally huddled, small semi-solid vomit seen in tray, passing urine.
		pm	Quiet but alert, occasionally active.
	4	am	Alert, occasionally active, passing urine.
		pm	Alert and active.
	5	am	Quiet but alert, dark faeces/pale loose faeces.
		pm	Quiet but alert, occasionally huddled, hunched posture, sitting on cage floor, no faeces seen.
	6	am	Quiet but alert, occasionally huddled, abdomen appears slightly swollen, no faeces seen.
		pm	Condition deteriorating, gross distension of abdomen causing considerable discomfort. Sacrificed due to poor clinical condition.
W704f	1	am	Quiet but alert, vomit in tray, faeces passed, minimal urine output.
		pm	Quiet, heavy lidded, becomes alert when stimulated, normal faeces.
	2	am	Alert, reasonably active, dark faeces, no urine.
		pm	Quiet but alert, occasionally huddled, dark faeces.
	3	am	Quiet but alert, dark faeces, seen picking at wound.
		pm	Quiet but alert, no faeces seen.
	4	am	Quiet but alert, loose/normal faeces.
		pm	Quiet but alert, loose faeces.
	5	am	Quiet but alert, no faeces, urinating, area around wound swollen
		pm	Quiet but alert, reasonably bright when motivated.
	6	am	Alert and active, grooming.
		pm	Alert and active, grooming.
	7	am	Alert and active, loose faeces.
		pm	Alert and active.
	8	am	Alert and active.
		pm	Alert and active, normal faeces.
	9	am	Alert and active, dark faeces.
		pm	Alert and active, dark faeces.
	10	am	Quiet but alert, occasionally active, dark faeces.
		pm	Quiet, huddled, subdued, little activity detected.
	11	am	Quiet but alert, occasionally active, sometimes huddled, dark faeces.
		pm	Quiet but alert, occasionally active, sometimes huddled, dark faeces.
	12	am	Quiet but bright and alert, dark faeces
		pm	Quiet but alert, normal faeces.
	13	am	Quiet but alert.
		pm	Quiet but alert, no faeces seen.

APPENDIX 11

(Individual clinical signs - continued)

Animal No./sex	Day No.		Observation
W704f (cont'd)	14	am	Alert and fairly active, normal faeces.
		pm	Quiet, huddled on perch, appears asleep.
	15	am	Quiet but alert, dark faeces.
		pm	Quiet but alert, no faeces seen.
	16	am	Quiet but alert.
		pm	No signs recorded.
	17	am	Quiet but alert.
		pm	Quiet but alert.
	18	am	Quiet but alert.
		pm	Quiet but alert. Kidney feels swollen, but animal bright and urinating.
	19	am	Alert and active, normal faeces.
		pm	Quiet but alert, loose faeces.
	20	am	Quiet but fairly active, diet vomit in tray.
		pm	Quiet but alert, normal faeces, diet vomit at dosing.
	21	am	Quiet but active and alert.
		pm	Quiet but active and alert.
	22	am	Quiet but alert, occasionally huddled.
		pm	Quiet, lying on ladder but active if approached.
	23	am	Quiet, huddled but alert.
		pm	Quiet, huddled but active if disturbed.
	24	am	Quiet, huddled but occasionally alert.
		pm	Quiet but alert, sits on perch and shows occasional movement.
	25	am	Quiet, huddled.
		pm	Quiet, huddled but active if disturbed, vomit in tray.
	26	am	Quiet, huddled, slow movements.
		pm	Quiet, huddled, slow movements.
	27	am	Quiet, huddled, slow movements and vocalising.
		pm	Quiet, huddled, slow movements. Adopting unusual stance in cage, possibly indicative of pain.
	28	am	Quiet, huddled, slow movements if disturbed, vomit and urine in tray.
		pm	Quiet, huddled, slow movements, no faeces passed.
	29	am	Quiet, huddled, appears asleep, loose faeces. Sacrificed due to poor condition and possible renal failure.
W755m	1	am	Quiet but alert, faeces passed, urine blood stained.
		pm	Quiet but alert, no faeces seen.
	2	am	Quiet but alert, dry blood along wound, passing urine..
		pm	Quiet but alert, wound seeping slightly, normal faeces.
	3	am	Quiet but alert, dry blood around wound, dark faeces.
		pm	Quiet but alert, picking at wound, dark/normal faeces.
	4	am	Quiet but alert, dry blood around wound, loose faeces, semi-digested vomit in tray.
		pm	Quiet but alert.
	5	am	Quiet but alert, dark faeces, semi-digested vomit in tray, passing urine.
		pm	Quiet but alert.
	6	am	Quiet but alert.
		pm	Quiet but alert and fairly active.
	7	am	Quiet but alert, loose faeces.
		pm	Quiet but alert.
	8	am	Quiet but alert, passing urine.
		pm	Quiet but alert, loose faeces.

APPENDIX 11

(Individual clinical signs - continued)

Animal No./sex	Day No.		Observation
W755m (continued)	9	am	Alert and active, dark faeces.
		pm	Alert and active, occasionally huddled, loose faeces.
	10	am	Alert and active, occasionally quiet, normal faeces.
		pm	Alert but quiet, showing gentle activity.
	11	am	Alert and occasionally active, observed picking wound, loose faeces
		pm	Alert and occasionally active, observed picking would, loose faeces.
	12	am	Quiet, huddled but alert, normal faeces.
		pm	Quiet, huddled but alert.
	13	am	Alert and active, loose faeces.
		pm	Quiet but alert, no faeces seen.
	14	am	Quiet but alert, huddled on perch, normal faeces.
		pm	Quiet, huddled on perch, appears asleep.
	15	am	Quiet but alert, dark faeces.
		pm	Quiet but alert, dark faeces.
	16	am	Quiet and huddled but alert.
		pm	No signs recorded.
	17	am	Quiet but alert.
		pm	Quiet but alert.
	18	am	Quiet but alert.
		pm	Quiet but alert, occasionally huddled, loose faeces.
	19	am	Quiet but alert, vomit in tray, liquid faeces.
		pm	Quiet but alert.
	20	am	Quiet but alert, loose/liquid faeces.
		pm	Quiet but alert, no faeces seen.
	21	am	Quiet but alert, responds to external stimuli.
		pm	Quiet but alert, responds to external stimuli.
	22	am	Quiet but alert, occasionally huddled, normal faeces.
		pm	Quiet but alert, sitting on perch, gentle activity.
	23	am	Quiet but alert, huddled, small vomit in tray.
		pm	Quit but alert, huddled, no faeces seen.
	24	am	Quiet, huddled, occasionally alert, loose faeces, wound slightly open.
		pm	Quiet, huddled, alert when stimulated, swelling under both eyes.
	25	am	Quiet, huddled, wound open, normal faeces.
		pm	No signs recorded.
	26	am	Quiet and huddled, wound open and moist, loose faeces.
		pm	Quiet, huddled and reluctant to move.
	27	am	Huddled and vocalising, wound normal.
		pm	Quiet, huddled and reluctant to move.
	28	am	Quiet and huddled, loose faeces.
		pm	Quiet and huddled, no faeces seen.
	29	am	Quiet and huddled, normal faeces.
		pm	No signs recorded.
	30	am	Quiet and huddled on perch, appears asleep.
		pm	Sacrificed due to poor clinical condition.
W526f	1	am	Occasionally lying on cage floor, quiet but alert, normal faeces.
		pm	No signs recorded.
	2	am	Quiet and huddled on perch, alert if disturbed.
		pm	Quiet and huddled on perch, alert if disturbed.

APPENDIX 11

(Individual clinical signs - continued)

Animal No./sex	Day No.		Observation
X526f (continued)	3	am	Quiet and lying on cage floor, alert if disturbed. Causing serious concern having shown lateral recumbency for greater part of the night.
		pm	No improvement. Sacrificed due to poor clinical condition
X533f	1	am	Quiet, huddled, eyes closed and leaning against perch, no faeces seen.
		pm	Quiet, huddled, eyes closed and leaning against perch, no faeces seen.
	2	am	Quiet and huddled, no faeces seen.
		pm	Quiet and huddled, no faeces seen.
	3	am	Quiet but alert, sitting at top of ladder, normal faeces .
		pm	Quiet and huddled, sitting on ladder and reluctant to move, vomit in tray, no faeces seen.
	4	am	Quiet but alert, sitting huddled on perch, vomit in tray, showing slight discomfort.
		pm	Quiet but alert, sitting huddled on perch, slow movements, normal faeces, vomit in tray .
	5	am	Quiet and huddled, sitting on perch, loose/liquid faeces, vomit in tray.
		pm	Quiet and huddled, dark faeces.
	6	am	Quiet and huddled on perch, normal faeces, vomit in tray.
		pm	Quiet and huddled on perch.
	7	am	Intermittently lying down. Sacrificed due to poor clinical condition.

APPENDIX 11

Individual clinical signs

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1).

APPENDIX 11

(Individual clinical signs - continued)

Animal No./sex	Day No.		Observation
X538f	1	am	Subdued, sitting on perch at back of cage, becomes alert when stimulated. Small amount of normal faeces.
		pm	Quiet but alert, sitting on cage floor, reluctant to move. No faeces seen.
	2	am	Quiet but alert, occasionally subdued, moves when approached. Small amount of normal faeces.
		pm	Alert, moving slowly along perch. Small amount of dark faeces.
	3	am	Subdued but active if stimulated, sitting on cage floor leaning against perch. Normal faeces.
		pm	Subdued but active if stimulated, sitting on cage floor leaning against perch. Normal faeces.
	4	am	Slightly subdued, fairly active, vocalising. Dark faeces. Vomit in tray
		pm	Quiet, huddled but alert. No faeces seen.
	5	am	Quiet, little movement. Normal faeces.
		pm	Quiet, reluctant to move, reasonably alert. Dark faeces.
	6	am	Slightly subdued. No faeces seen.
		pm	Quiet but alert.
	7	am	Slightly subdued. No faeces seen.
		pm	Quiet and huddled on perch, becomes alert when stimulated. Normal faeces.
	8	am	Very quiet, sitting on cage floor, huddled but alert, appears tired.
		pm	Quiet, lying on cage floor, becomes alert when stimulated. Slow to stand up, appears weak. Small bruises on face. No faeces seen.
	9	am	Lying down or sitting hunched with head down. Petechial haemorrhages all over body. Sacrificed on humane grounds.
X539f	1	am	Quiet but alert, lying on cage floor. No faeces seen.
		pm	Quiet but alert, sitting on perch, moves when approached. No faeces seen.
	2	am	Quiet, lying on ladder, eyes nearly closed, becomes alert and moves when approached. Small amount of dark faeces.
		pm	Quiet but alert, sitting on perch. No faeces seen.
	3	am	Subdued , sitting/lying on ladder, alert and active only if stimulated. No faeces seen.
		pm	Subdued , sitting/lying on ladder, alert and active only if stimulated. No faeces seen.
	4	am	Alert and active. Dark/normal faeces.
		pm	Quiet and huddled but alert. Dark faeces.
	5	am	Quiet and huddled, alert when stimulated. Slightly loose faeces.
		pm	Quiet and huddled, alert when stimulated. No faeces seen.
	6	am	Alert and slightly subdued. No faeces seen.
		pm	Quiet but alert. Lying across perch, eyes closed.
	7	am	Slightly subdued. No faeces seen. Vomit in tray.
		pm	Very quiet and huddled, becomes alert when stimulated though reluctant to move. Occasionally lies on cage floor. General piloerection. Swelling around both eyes. Liquid faeces.
	8	am	Quiet and huddled, little movement, little response to stimuli. Puffiness above eyes. Loose faeces. No urine passed.
		pm	Sitting on cage floor, seems tired. Swelling around eyes more pronounced. General piloerection. Liquid faeces.
	9	am	Sacrificed due to poor condition, petechial haemorrhage on eyelids, arms and chest, generalised subcutaneous oadema and lack of urine potput..

APPENDIX 11

(Individual clinical signs - continued)

Animal No./sex	Day No.		Observation
X540f	1	am	Quiet, sitting on floor in corner of cage, eyes closed, appears reluctant to move. No faeces seen.
		pm	Lying on cage floor, sits up when approached, reluctant to move and then only slowly. General piloerection. Dark faeces.
	2	am	Quiet but alert, reluctant to move, appears weak when moving. Loose faeces.
		pm	Quiet but alert, slightly subdued, sitting on perch. No faeces seen.
	3	am	Subdued, sitting on perch, reluctant to move when stimulated. No faeces seen.
		pm	Fairly active. No faeces seen.
	4	am	Slightly subdued, sitting on cage floor. No faeces seen.
		pm	Quiet, huddled but alert. No faeces seen.
	5	am	Alert, sitting on cage floor. No faeces seen.
		pm	Alert, sitting on ladder. Loose faeces.
	6	am	Subdued, at back of cage on floor. Loose faeces.
		pm	Quiet but alert. Loose faeces.
	7	am	Very quiet, laying on cage floor. Appears to have colic and is concurrently diarrhoeic. Haemorrhages in skin. No faeces seen.
		pm	Appears asleep on perch, becomes alert when stimulated. Small bruises on skin mainly on face, back and abdomen. No faeces seen.
	8	am	Laying on cage floor, reluctant to move. Generalised bruising all over body. Loose faeces.
		pm	Very quiet and huddled, sitting on perch, becomes alert when stimulated. Generalised bruising, especially on face. No faeces seen.
	9	am	Found in a collapsed state. Petechiae all over body, bloody froth at nose. Sacrificed for humane reasons.
X665m	1	am	Very quiet, laying on cage floor, little response to stimuli. Dehydrated. Normal faeces.
		pm	Laying on cage floor, rises to perch when stimulated, appears tired, eyes half closed. No faeces seen.
	2	am	Sitting on perch, leaning against ladder, subdued, reluctant to move even when stimulated. Dark faeces.
		pm	Sitting on ladder or crouched on floor, subdued but alert. Loose faeces containing mucus.
	3	am	Very quiet, sitting on perch, not very active. No faeces seen.
		pm	Lying on ladder but alert. Normal faeces.
	4	am	Quiet and huddled on ladder, becomes alert when stimulated, reluctant to move. Dark faeces. Vomit in tray.
		pm	Quiet but alert.
	5	am	Quiet but alert. Loose faeces.
		pm	Quiet and huddled, becomes alert when approached. Loose faeces.
	6	am	No comment made on animal condition.
		pm	Quiet but alert. Dark/loose faeces.
	7	am	Quiet and huddled on perch. Appears dehydrated.
		pm	Quiet and huddled on perch. Dark/loose faeces.
	8	am	Very quiet and inactive, laying on cage floor. Little response to stimuli. Petechial haemorrhages in skin. Possible vomit in tray.
		pm	Found in collapsed state. Sacrificed for humane reasons

APPENDIX 11

(Individual clinical signs- continued)

Animal No./sex	Day No.		Observation
X657m	1	am	Very quiet, laying on cage floor, little response to stimuli. Dehydrated. Some faeces seen.
		pm	Laying on cage floor, rises to an unusual posture when approached. Dark faeces.
	2	am	Slightly subdued, laying down or sitting hunched with head down, active if stimulated.. Normal faeces.
		pm	Sitting on ladder or crouched on cage floor, alert if stimulated.. No faeces seen.
	3	am	Quiet but alert, also lying face down on cage floor. No faeces seen.
		pm	Subdued and huddled on perch. No faeces seen.
	4	am	Quiet but alert. Very pale, hunched posture, unusual posture laying on ladder, moves when stimulated. Dark faeces. Vomit in tray.
		pm	Quiet but alert.
	5	am	Quiet but alert, sitting on perch. Dark faeces.
		pm	Quiet but alert, sitting on perch. Loose faeces.
	6	am	Quiet but alert, sitting on perch. Loose faeces.
		pm	Quiet but alert, sitting on perch, occasionally huddled. Loose faeces.
	7	am	Quiet and huddled on perch., appears uncomfortable on movement, peculiar posture. Loose faeces.
		pm	Quiet and huddled, sitting on cage floor, becomes alert when stimulated. No faeces seen.
	8	am	Quiet and huddled but alert. No faeces seen.
		pm	No comment made on animal condition.
	9	am	Quiet but alert, sitting on perch. Dark loose faeces.
		pm	Quiet but alert, huddled at back of cage.
	10	am	Subdued and huddled on perch, reluctant to move. Face appears bruised. No faeces seen.
		pm	Alert and fairly active. Face appears bruised. No faeces seen.
	11	am	Slightly subdued, standing on all fours, slow when moving. Normal faeces.
		pm	Alert and occasionally active.
	12	am	Subdued and huddled on perch, reluctant to move, eyes closed. No faeces seen. Collapsed in dorsal recumbency when being handled, unaware of surroundings, shallow breathing and very weak pulse. Petechial haemorrhage on skin. Sacrificed on humane grounds.
X535f	1	am	Quiet and huddled on perch, reluctant to move.
		pm	Quiet and huddled on perch, reluctant to move. No faeces seen.
	2	am	Alert and active, heavy lidded, slightly unsteady. Abdomen slightly distended and subcutaneous haemorrhage/bruising noted on anus. Normal faeces.
		pm	Appears weak when moving, reluctant to move but alert when stimulated. No faeces seen.
	3	am	Quiet but alert. Heavy generalised bruising over body. Some faeces seen.
		pm	Quiet, little movement, huddled on perch.
	4	am	Quiet, sitting on perch. No faeces seen.
		pm	Quiet and huddled on ladder but alert. No faeces seen.
	5	am	Subdued, heavy lidded, sitting on perch, slight body tremors. Weak and very severely bruised. No faeces seen.
		pm	Subdued, heavy lidded, sitting on perch, slight body tremors. Weak, slightly unsteady when moving. Very severely bruised. No faeces seen
	6	am	Found dead on cage floor.

APPENDIX 11

(Individual clinical signs - continued)

Animal No./sex	Day No.		Observation
X659m	1	am	Quiet and huddled on perch, eyes shut, reluctant to move.
		pm	Quiet but alert, sitting on cage floor, reluctant to move. No faeces seen.
	2	am	Quiet, huddled, head between legs, no activity. No faeces seen.
		pm	Laying on cage floor, sits up when stimulated. Very little urine passed.
	3	am	Quiet but alert, huddled, little movement. Dark faeces.
		pm	Quiet and huddled, little movement.
	4	am	Quiet but alert, sitting on cage floor. No faeces seen.
		pm	Quiet but alert. No faeces seen.
	5	am	Slightly subdued, sitting huddled on cage floor, alert if stimulated. Normal faeces. Urine production minimal, extremely oedematous.
		pm	Sacrificed for humane reasons.
X666f	1	am	Alert and fairly active. No faeces seen.
		pm	Alert and occasionally active. No faeces seen.
	2	am	Alert and fairly active. No faeces seen.
		pm	Quiet but alert, huddled, lying across perch. No faeces seen.
	3	am	Quiet but alert. No faeces seen.
		pm	Alert and fairly active. No faeces seen.
	4	am	Subdued but alert, reluctant to move
		pm	Slightly subdued but alert if stimulated. Normal faeces.
	5	am	Subdued but alert, sitting on perch.
		pm	Very quiet and subdued. Nystagmus evident. No urine passed overnight. Sacrificed for humane reasons.
X663m	1	am	Subdued and huddled on cage floor. Normal faeces.
		pm	Quiet but alert, sitting on cage floor. No faeces seen.
	2	am	Subdued but alert, sitting hunched on ladder. Movement slow. Very little urine passed. Normal faeces.
		pm	Subdued, lying across perch or on ladder. No faeces seen.
	3	am	Quiet, hunched on ladder, reluctant to move. Still not passing urine even after diuretic treatment. No faeces seen.
		pm	Subdued, sitting on perch. Not passing urine. Loose faeces.
	4	am	Subdued, lying on perch, reluctant to move. Not passing urine. Sacrificed for humane reasons.
X660f	1	am	Slightly subdued, fairly active if stimulated. No faeces seen.
		pm	Quiet and huddled, sitting on ladder. No faeces seen.
	2	am	Slightly subdued, fairly active if stimulated. Urine output poor. Loose faeces.
		pm	Subdued and reluctant to move.
	3	am	Quiet but alert and active if approached. Urinating well.
		pm	Quiet but alert, reluctant to move. Liquid faeces.
	4	am	Quiet but alert, laying on cage floor. Slightly weak. Liquid faeces.

APPENDIX 11

(Individual clinical signs - continued)

Animal No./sex	Day No.		Observation
X660f (contd)	4	pm	Very quiet and huddled but alert, slumped on perch and ladder. Urine output very poor.
	5	am	Quiet and huddled but alert. Some puffiness around eyes. Liquid faeces.
		pm	Quiet, huddled on perch. Clotted blood around wound.
	6	am	Quiet and huddled. Abdomen tender, bleeding from wound. May not be urinating. No faeces seen.
		pm	Quiet and huddled on perch. No faeces seen.
	7	am	Quiet. Vomit in tray. Liquid faeces.
		pm	Quiet but alert, sitting on perch. Vomit in tray. No faeces seen.
	8	am	Quiet, huddled on ladder. Puffy eyes. Vomit in tray. Loose/liquid faeces.
		pm	Quiet but alert, sitting on perch. No faeces seen.
	9	am	Subdued, huddled. Puffy eyes. Loose faeces. Sacrifice for humane reasons.
X661m	1	am	Alert and active if stimulated. Vomit in tray. Normal faeces.
		pm	Quiet but alert, becomes active when stimulated. Small amount of normal faeces.
	2	am	Alert and active if stimulated. Urine output poor. No faeces seen.
		pm	Alert and active if approached.
	3	am	Quiet but alert and active. Urinating well. No faeces seen.
		pm	Quiet but alert and active. No faeces seen.
	4	am	Quiet but alert, bright and active. Normal faeces.
		pm	Quiet, active and responsive.
	5	am	Quiet but alert. Normal faeces.
		pm	Quiet, peculiar posture, lying on perch, appears to be retching.
	6	am	Quiet but alert. Liquid faeces.
		pm	Quiet but alert. Liquid faeces.
	7	am	Quiet but alert. Normal faeces.
		pm	Quiet but alert, sitting on ladder.
	8	am	Slightly subdued but bright, alert if stimulated. Normal faeces.
		pm	Quiet but alert. Very loose faeces.
	9	am	Subdued, lying on perch, reluctant to move. Loose faeces. Petechiae all over body. Sacrificed for humane reasons
X662f	1	am	Subdued and depressed, reluctant to move even if stimulated, sitting in upright position. Normal faeces.
		pm	Very quiet and subdued, sitting on cage floor, reluctant to move. Eyes partially closed.
	2	am	Subdued, reluctant to move if stimulated, looking miserable, sitting in upright position. Urine output poor. No faeces seen.
		pm	Subdued, reluctant to move, huddled on cage floor.
	3	am	Looking miserable, huddled and hunched on cage floor, reluctant to move. Very poor urine output. No faeces seen.
		pm	Sacrificed for humane reasons.

APPENDIX 11

Individual clinical signs

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1) unless the animal failed to survive Day 0.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
W337m	1	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert, lying on cage floor. No faeces seen.
	2	am	Lying on cage floor, reluctant to move, unsteady. Alert and aggressive if stimulated. Blood around penis. Pale mucous membranes.
		pm	Sacrificed for humane reasons.
X655m	1	am	04.00 Animal died.
X658f	1	am	Quiet but alert.
		pm	Quiet but alert and active, moving in cage and sitting on ladder. Urine passed.
	2	am	Slightly subdued but active if stimulated.
		pm	Quiet but alert. No faeces seen.
	3	am	Subdued but alert.
		pm	Subdued but alert. Normal faeces.
	4	am	Slightly subdued but alert if stimulated, sitting on perch. Urinating well..
		pm	Subdued and huddled on perch. No faeces seen
	5	am	Subdued and huddled on perch. Normal faeces.
		pm	Subdued and huddled on perch. No faeces seen.
	6	am	Quiet but alert, sitting on perch.
		pm	Quiet and huddled, slow movements if stimulated. Normal faeces.
	7	am	Slightly subdued, alert if stimulated, slow movements.
		pm	Alert at front of cage, quiet. No faeces seen.
	8	am	Quiet but alert if stimulated. Loose faeces.
		pm	Quiet but alert, sitting on perch. No faeces seen.
	9	am	Alert but very quiet. No faeces seen.
		pm	Sacrificed for humane reasons.
X395m	1	am	Quiet but alert. No faeces seen.
		pm	Quiet, sitting on perch, slightly alert. No faeces seen.
	2	am	Quiet, sitting on perch, slightly alert. No faeces seen.
		pm	Quiet but alert. No faeces seen.
	3	am	Subdued but alert. No faeces seen.
		pm	Subdued and huddled, becomes alert when stimulated but reluctant to move.
	4	am	Quiet and huddled. Faeces passed.
		pm	Quiet and huddled on perch, alert if stimulated.
	5	am	Quiet and huddled on perch, alert if stimulated.
		pm	Quiet and huddled on perch, alert if stimulated. No faeces seen.
	6	am	Quiet but alert, sitting on perch. Normal faeces.
		pm	Quiet but alert, sitting on cage floor at front of cage.
	7	am	Quiet but alert, occasionally active.
		pm	Slightly subdued, sitting on perch, moves when stimulated. No faeces seen.
	8	am	Quiet but alert, sitting on perch. Normal faeces.
		pm	Quiet but alert, sitting on cage floor.
	9	am	Quiet but alert, slow movements when active.
		pm	Quiet but alert, reluctant to move. No faeces seen.
	10	am	Quiet but alert, slow movements when active. Normal faeces.
		pm	Quiet but alert, slow movements when active.
	11	am	Quiet but alert, slow movements when active.
		pm	Quiet but alert, slow movements when active.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
X395m (contd)	12	am	Quiet but alert.
		pm	Quiet but alert. Dry scabs on right side of face and right arm.
	13	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert. Dry scabs on right side of face and right arm.
	14	am	Quiet but alert, sitting on perch. Small amount of normal faeces passed.
		pm	Quiet but alert.
	15	am	Quiet but alert, sitting on perch, moves when stimulated.
		pm	Quiet but alert.
	16	am	Quiet but alert.
		pm	Records not completed
	17	am	Quiet but alert.
		pm	Quiet but alert, occasionally active.
	18	am	Subdued but alert.
		pm	Subdued but alert.
	19	am	Subdued but alert.
		pm	Subdued but alert.
	20	am	Quiet but alert and bright.
		pm	Quiet but alert.
	21	am	Quiet but alert. Loose faeces.
		pm	Quiet but alert. Slow movements when stimulated. Loose faeces.
	22	am	Quiet but alert. Normal faeces.
		pm	Alert and active.
	23	am	Alert and active.
		pm	Alert and active.
	24	am	Alert and active.
		pm	Quiet but alert, slow movements when active.
	25	am	Quiet and huddled on ladder.
		pm	Quiet but alert.
	26	am	Quiet but alert when stimulated.
		pm	Quiet but alert, sitting on perch. Small vomit in tray.
	27	am	Quiet but alert.
		pm	Quiet but alert, huddled on perch.
	28	am	Quiet but alert, slow when moving.
		pm	Quiet but alert, slow when moving.
	29	am	Quiet but alert, huddled on perch.
		pm	Quiet but alert.
	30	am	Quiet but alert, slow when moving. Slight localised reaction to stitch at lower end of wound.
		pm	Alert.
	31	am	Quiet and huddled but alert. Loose faeces.
		pm	Quiet and huddled but alert and active. Loose faeces.
	32	am	Quiet and huddled. Loose faeces.
		pm	Quiet and huddled. Loose faeces.
	33	am	Quiet and huddled on perch. Normal faeces.
		pm	Quiet and huddled on perch.
	34	am	Quiet and huddled on perch.
		pm	Quiet and huddled on perch. Abdomen and scrotal sac swollen.
	35	am	Alert and active.
		pm	Quiet but alert.

APPENDIX 11

Individual clinical signs

Animal no./sex	Day no.		Observation
X395m (contd)	36	am	Quiet but alert.
		pm	Quiet but alert.
	37	am	Quiet but alert.
		pm	Quiet but alert.
	38	am	Alert and active.
		pm	Quiet but alert.
	39	am	Quiet and huddled on perch or ladder.
		pm	Quiet and huddled on perch or ladder, reluctant to move. Vocalising.
	40	am	Quiet but alert. Subcutaneous swelling around abdominal wound, soft and painless.
		pm	Quiet but alert.
	41	am	Quiet but alert, active when stimulated.
		pm	Quiet but alert, active when stimulated.
	42	am	Quiet and huddled on perch.
		pm	Quiet and huddled on perch, fairly active, slow movements.
	43	am	Quiet but alert, fairly active.
		pm	Quiet but alert, fairly active. Subcutaneous swelling around wound increased in size.
	44	am	Quiet but alert.
		pm	Quiet but alert, huddled at times.
	45	am	Quiet and huddled on perch.
		pm	Quiet and huddled on perch.
	46	am	Quiet and huddled on ladder.
		pm	Quiet and huddled on ladder.
	47	am	Quiet and huddled on perch.
		pm	Quiet and huddled on perch.
	48	am	Quiet but alert, fairly active. Vomit in tray.
		pm	Quiet but alert, fairly active. Vomit in tray.
	49	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert. Vomit in tray.
	50	am	Quiet and huddled. Increase in swelling around abdominal wound, left side fluid filled, right side soft.
		pm	Quiet and huddled.
	51	am	Quiet and huddled, head between legs.
		pm	Quiet and huddled.
	52	am	Quiet but alert, huddled on perch.
		pm	Quiet and huddled on perch, becomes alert when stimulated. Slight swelling under both eyes.
	53	am	Quiet and huddled on perch.
		pm	Quiet and huddled on perch, fairly active. Observed vomiting.
	54	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert, sitting on perch.
	55	am	Quiet and huddled, little or no movement.
		pm	Quiet and huddled, little or no movement.
	56	am	Quiet but alert. Sacrificed for humane reasons.
X664f	1	am	Quiet and huddled, alert if stimulated. No faeces seen.
		pm	Quiet but alert, active when stimulated. No faeces seen.
	2	am	Quiet but alert, active when stimulated. No faeces seen.
		pm	Subdued and lying on cage floor. No faeces seen.

APPENDIX 11

Individual clinical signs

Animal no./sex	Day no.		Observation
X664f	3	am	Subdued, sitting on perch, reluctant to move when stimulated. Showing discomfort associated with abdomen. Loose faeces.
		pm	Subdued, occasionally lying on cage floor, sits on perch when stimulated. Abdomen swollen. No faeces passed.
	4	am	Sacrificed for humane reasons.
W50f	1	am	Quiet, sitting upright on perch. No faeces seen.
		pm	Quiet, sitting upright on perch. No faeces seen.
	2	am	Quiet but alert. Normal faeces. Vomit in tray.
		pm	Quiet and huddled, appears asleep. No faeces seen.
	3	am	Quiet but alert, sitting on cage floor. Normal faeces. Vomit.
		pm	Quiet but alert, sitting on perch.
	4	am	Quiet but alert, huddled on cage floor. No faeces seen. Vomiting profusely and continuously.
		pm	Quiet but alert, huddled on cage floor appears more alert than earlier. No faeces or vomit seen.
	5	am	Quiet and huddled on cage floor. No faeces seen. Vomited whilst being bled.
		pm	Sacrificed because of abnormal biochemistry findings.
X520f	1	am	Quiet and huddled, little or no response to stimulation. Normal faeces.
		pm	Quiet, responding to stimulation.
	2	am	Quiet but alert, hunched and reluctant to move.
		pm	Quiet but alert. No faeces seen.
	3	am	Quiet but alert, sitting on cage floor. Abdomen obviously uncomfortable and extremely tense, adopting abnormal stance on cage floor. Slightly dehydrated. Normal faeces. Small vomit. Good urine output.
		pm	Quiet but alert, sitting on perch. Appears unstable and tender.
	4	am	Very subdued, lying on cage floor, shallow breathing, body and limb tremors. Subsequently collapsed. Sacrificed for humane reasons.
X530f	1	am	Quiet but alert. Normal faeces.
		pm	Quiet but alert.
	2	am	Quiet but alert..
		pm	Quiet but alert. No faeces seen.
	3	am	Quiet but alert, sitting on perch. No faeces seen. Good urine output.
		pm	Quiet but alert. Observed vomiting.
	4	am	Alert, active if stimulated. No faeces seen. Vomit in tray.
		pm	Quiet and huddled on perch. Dark faeces.
	5	am	Alert and aggressive. Dark faeces.
		pm	Alert and aggressive. Appears tender in abdominal area.
	6	am	Alert and active. Dark faeces. Urinated well overnight.
		pm	Alert and active. Normal faeces.
	7	am	Quiet and huddled but alert.
		pm	Quiet and huddled but alert. No faeces seen.
	8	am	Quiet but alert, sitting at top of ladder. Normal faeces.
		pm	Alert and active. No faeces seen.
	9	am	Quiet but alert, sitting on ladder. Dark faeces.
		pm	Quiet but alert, sitting on perch.
	10	am	Quiet but alert, sitting in hammock. Dark faeces.
		pm	Quiet but alert, sitting in hammock. No faeces seen.

APPENDIX 11

Individual clinical signs

Animal no./sex	Day no.		Observation
X530f (contd)	11	am	Very quiet, appears tired, laying in hammock. Normal faeces.
		pm	Quiet but alert. Dark faeces.
	12	am	Quiet but alert. Normal faeces.
		pm	Quiet but alert. No faeces seen.
	13	am	Quiet but alert, sitting at top of ladder. Normal faeces.
		pm	Quiet but alert, sitting at top of ladder.
	14	am	Alert and active.
		pm	Alert and active.
	15	am	Quiet but alert, fairly active.
		pm	Quiet but alert, fairly active.
	16	am	Quiet but alert and bright, fairly active.
		pm	Quiet but alert, fairly active.
	17	am	Alert and active. No faeces seen.
		pm	Alert and active. No faeces seen.
	18	am	Quiet and huddled on ladder, becomes alert and aggressive when stimulated. Slight swelling above eyes. Normal faeces.
		pm	Quiet but alert.
	19	am	Quiet, laying in hammock. Loose faeces.
		pm	Quiet, laying in hammock. No loose faeces seen.
	20	am	Quiet but alert, occasionally active. Normal faeces.
		pm	Quiet but alert, occasionally active.
	21	am	Quiet but alert.
		pm	Quiet but alert, laying in hammock.
	22	am	Quiet but alert and active.
		pm	Quiet but alert and active.
	23	am	Quiet but alert, sitting in hammock.
		pm	Quiet but alert and active, sitting on ladder, threatening.
	24	am	Alert and fairly active.
		pm	Alert and fairly active.
	25	am	Alert, some activity, occasionally lying in hammock.
		pm	Alert, some activity, occasionally lying in hammock.
	26	am	Alert and fairly active. Loose faeces.
		pm	Quiet but alert, sitting on perch, threatening when stimulated.
	27	am	Quiet but alert, sitting on ladder. Loose faeces.
		pm	Quiet but alert and active, sitting on ladder.
	28	am	Alert and active. Slightly loose faeces.
		pm	Alert and active. No faeces seen
	29	am	Quiet but alert. Normal faeces.
		pm	Quiet but alert, sitting in hammock. No faeces seen.
	30	am	Quiet but alert, active if stimulated. Pale loose faeces.
		pm	Quiet but alert, laying in hammock. No loose faeces seen.
	31	am	Quiet but alert, sitting on ladder, active if stimulated. Loose/normal faeces.
		pm	Quiet but alert and active, threatening when stimulated.
	32	am	Quiet but alert, sitting on perch. Normal faeces.
		pm	Quiet but alert, sitting on perch, threatening when stimulated.
	33	am	Alert, active and aggressive. No faeces seen.
		pm	Quiet but alert and active, sitting on perch
	34	am	Alert and active. Loose faeces.
		pm	Alert and active. Loose faeces.
	35	am	Alert and active. Pale, loose faeces.
		pm	Alert and active. Liquid faeces.

APPENDIX 11

Individual clinical signs

Animal no./sex	Day no.		Observation
X530f (contd)	36	am	Alert and fairly active. Loose/liquid faeces.
		pm	Alert and fairly active. Loose/liquid faeces.
	37	am	Alert and active. Loose/liquid faeces.
		pm	Alert and active, brighter. Well hydrated. Loose faeces.
	38	am	Alert and active. Loose faeces.
		pm	Alert and active. No faeces seen.
	39	am	Alert and active. Pale faeces.
		pm	Quiet, huddled but alert. No faeces seen.
	40	am	Quiet but alert, threatening and active when stimulated. Hard faeces.
		pm	Quiet but alert, threatening and active when stimulated. Hard faeces.
	41	am	Alert and active. Pale faeces.
		pm	Alert and active. Pale faeces.
	42	am	Quiet but alert, occasionally active. No faeces seen.
		pm	Quiet but alert, active when stimulated. Normal faeces.
	43	am	Quiet but alert and bright, sometimes active.
		pm	Quiet but alert, sometimes active.
	44	am	Quiet but alert. Loose faeces.
		pm	Quiet but alert. Normal faeces.
	45	am	Alert and active.
		pm	Alert and active.
	46	am	Quiet but alert, sitting in hammock. Pale faeces.
		pm	Quiet and huddled in hammock. Pale faeces.
	47	am	Quiet but alert, sitting in hammock. Normal faeces.
		pm	Quiet but alert, sitting in hammock. Fairly active, moving around cage.
	48	am	Quiet and subdued, sitting on ladder.
		pm	Alert and active. No faeces seen.
	49	am	Alert and active, sometimes quiet. Normal faeces.
		pm	Alert and active, sometimes quiet.
	50	am	Alert and fairly active around cage.
		pm	Alert and fairly active around cage.
	51	am	Alert, moving around cage.
		pm	Alert, moving around cage.
	52	am	Alert and active.
		pm	Quiet but alert.
	53	am	Quiet but alert, occasionally active.
		pm	Quiet but alert, occasionally active.
	54	am	Quiet but alert, active in cage.
		pm	Quiet but alert, active in cage.
	55	am	Quiet but alert, active in cage.
		pm	Quiet but alert, active in cage.
	56	am	Quiet but alert, occasionally active. Loose faeces.
		pm	Alert and active. Loose faeces.
	57	am	Quiet but alert, fairly active. Loose faeces.
		pm	Alert, moving around cage. Slightly loose faeces.
	58	am	Quiet but alert, fairly active. Loose faeces.
		pm	Quiet but alert, fairly active. Loose faeces.
	59	am	Quiet but alert, responds to external stimuli. Normal faeces.
		pm	Quiet but alert, moving around cage, responds to external stimuli.
	60	am	Quiet but alert, occasionally active.
		pm	Quiet but alert.

APPENDIX 11

Individual clinical signs

Animal no./sex	Day no.		Observation
X530f (contd)	61	am	Quiet, huddled on perch, eyes semi-closed.
		pm	Quiet but alert, occasionally active. No faeces seen.
	62	am	Quiet, sitting on perch. Normal faeces.
		pm	Quiet, sitting on perch.
	63	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert, huddled on perch. Appears heavy lidded.
	64	am	Sitting on perch, appears asleep.
		pm	Alert, fairly active, sitting on perch. No faeces seen.
	65	am	Quiet, huddled but alert. Abdomen appears extremely distended. Faeces seen.
		pm	Quiet but alert, huddled on ladder. Normal faeces.
	66	am	Quiet but alert, huddled on ladder. Abdomen distended.
		pm	Quiet but alert, huddled on ladder. Abdomen distended. No faeces seen.
	67	am	Quiet but alert, active when disturbed. Liquid faeces.
		pm	Alert and active, sitting on perch. Dark faeces.
	68	am	Quiet and huddled, little movement. Normal faeces.
		pm	Alert, sitting on ladder.
	69	am	Quiet and huddled but alert, active if approached.
		pm	Quiet but alert and slightly active, sitting on perch. Dark faeces.
	70	am	Quiet but fairly active. Normal faeces.
		pm	Quiet but alert, slightly active. Abdomen distended. No faeces seen. Vomit seen.
	71	am	Fairly active and alert.
		pm	Alert, occasionally active. Abdomen visibly distended. Normal faeces.
	72	am	Fairly active.
		pm	Quiet but active when stimulated.
	73	am	Quiet but alert. Abdomen very bloated (ascitic).
		pm	Quiet but alert. Abdomen very bloated.
	74	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert, sitting on perch.
	75	am	Alert and active.
		pm	Alert and active.
	76	am	Quiet but alert. Abdomen extremely distended.
		pm	Quiet but alert. Abdomen extremely distended. No faeces seen.
	77	am	Quiet and huddled on perch. Fluid aspirated under anaesthetic from distended abdomen. Normal faeces.
		pm	Recovering from sedation, sitting up.
	78	am	Very quiet but becomes alert if stimulated. No urine passed. Abdomen filling with fluid again.
		pm	Sacrificed for humane reasons.
X652f	1	am	Quiet but alert, huddled on perch. No faeces seen.
		pm	Quiet and huddled on perch but more alert and active than earlier.
	2	am	Quiet but alert, huddled, reluctant to move when stimulated. No faeces seen.
		pm	Quiet but alert. No faeces seen.
	3	am	Quiet but alert, sitting on perch. Huddled and appears uncomfortable. No faeces seen.
		pm	Quiet but alert, sitting on perch. No faeces seen.
	4	am	Subdued, fixed huddled crouched posture, reluctant to move. No faeces seen. Urine output good.
		pm	Subdued, fixed huddled crouched posture, reluctant to move. Mucous covered faeces passed.

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Individual clinical signs

Animal no./sex	Day no.		Observation
X652f (cont)	5	am	Quiet, huddled but alert, more active than previous day. Clear nasal discharge. Eyes appear sunken. Normal faeces.
		pm	Quiet, huddled but alert, more active than previous day. Clear nasal discharge. Eyes appear sunken.
	6	am	Quiet and huddled, posture indicative of abdominal discomfort, very pale and extremely subdued, reluctant to move. Slight body tremors. Loose faeces.
		pm	Sacrificed for humane reasons.
Y201m	1	am	Alert and fairly active. Normal faeces.
		pm	Quiet but alert, sometimes active.
	2	am	Quiet but alert, sometimes active.
		pm	Quiet but alert.
	3	am	Quiet but alert.
		pm	Alert and fairly active.
	4	am	Alert and fairly active.
		pm	Alert and fairly active.
	5	am	Quiet but alert, sometimes active. Vomit in tray.
		pm	Quiet but alert, sometimes active.
	6	am	Alert and active, moving around cage. Loose faeces.
		pm	Alert and active, moving around cage. Loose faeces.
	7	am	Alert and active. Normal faeces.
		pm	Quiet but alert, sitting on ladder. No faeces seen.
	8	am	Quiet but alert, sometimes active. Normal faeces.
		pm	Quiet but alert, sometimes active.
	9	am	Quiet but alert, huddled on perch.
		pm	Quiet but alert, huddled on perch.
	10	am	Alert and active.
		pm	Alert and active.
	11	am	Quiet but alert. Clear nasal discharge.
		pm	Quiet but alert.
	12	am	Quiet but alert, sometimes active.
		pm	Quiet but alert, moves when stimulated. No faeces seen.
	13	am	Quiet but alert, sitting on cage floor. Small amount of normal faeces.
		pm	Quiet but alert, sitting on cage floor.
	14	am	Quiet but alert, sitting on cage floor.
		pm	Quiet but alert, sitting on cage floor.
	15	am	Quiet but alert, occasionally active. Pale faeces.
		pm	Quiet but alert, fairly active. No faeces seen.
	16	am	Quiet but alert, fairly active.
		pm	Quiet but alert.
	17	am	Quiet but alert, fairly active.
		pm	Quiet but alert. Normal faeces.
	18	am	Quiet but alert, moving around cage.
		pm	Alert and active, moving around cage.
	19	am	Alert and active.
		pm	Quiet but alert. Dark faeces.
	20	am	Quiet but alert, sitting on perch. Normal faeces.
		pm	Quiet but alert, sitting on cage floor. No faeces seen.

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Individual clinical signs

Animal no./sex	Day no.		Observation
Y201m (contd)	21	am	Alert and fairly active. Normal faeces.
		pm	Alert and fairly active.
	22	am	Quiet but alert, sitting on ladder. Dark faeces.
		pm	Alert, sitting on perch. No faeces seen.
	23	am	Alert, sitting on perch. Normal faeces.
		pm	Alert and fairly active. No faeces seen.
	24	am	Quiet but alert. Dark faeces.
		pm	Quiet but alert, occasionally active. Normal faeces.
	25	am	Quiet but alert.
		pm	Quiet but alert, huddled on cage floor. No faeces seen.
	26	am	Quiet and huddled but alert, reluctant to move. Dark faeces.
		pm	Alert and slightly active, resting on ladder. No faeces seen.
	27	am	Quiet and huddled. Normal faeces.
		pm	Alert and active.
	28	am	Quiet and huddled on cage floor.
		pm	Alert and active.
	29	am	Quiet and huddled on cage floor, fairly active.
		pm	Alert and active, sitting on perch.
	30	am	Huddled but alert. Loose faeces.
		pm	Alert and active. No faeces seen.
	31	am	Alert and active, moving around cage. Normal faeces.
		pm	Alert and active, moving around cage.
	32	am	Quiet but alert. Loose faeces.
		pm	Quiet but alert. Normal faeces.
	33	am	Quiet but alert and active.
		pm	Quiet but alert and active.
	34	am	Quiet but alert.
		pm	Quiet but alert.
	35	am	Quiet but alert.
		pm	Alert and active. No faeces seen.
	36	am	Alert and active. Normal faeces.
		pm	Quiet but alert. No faeces seen.
	37	am	Alert and active. No faeces seen.
		pm	Alert and active. Normal faeces.
	38	am	Alert and active.
		pm	Alert and active. No faeces seen.
	39	am	Quiet and huddled but alert. Normal faeces.
		pm	Quiet and huddled but alert. No faeces seen.
	40	am	Quiet and huddled but alert.
		pm	Quiet but alert. No faeces seen.
	41	am	Quiet but alert. Loose faeces.
		pm	Quiet but alert. Loose faeces.
	42	am	Quiet but alert. Normal faeces.
		pm	Quiet but alert.
	43	am	Quiet but alert.
		pm	Quiet but alert. No faeces seen.
	44	am	Quiet but alert. Loose faeces.
		pm	Quiet but alert. Normal faeces.
	45	am	Quiet but alert.
		pm	Quiet but alert.

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Individual clinical signs

Animal no./sex	Day no.		Observation
Y201m (contd)	46	am	Quiet but alert, active when stimulated.
		pm	Quiet but alert, active when stimulated. Loose faeces.
	47	am	No abnormalities detected. Aggressive. Loose faeces.
		pm	Quiet and huddled. Loose faeces.
	48	am	Quiet but alert, sitting on perch. Dark faeces.
		pm	Quiet but alert. No faeces seen.
	49	am	Quiet and huddled. Abdomen enlarged. Normal faeces.
		pm	Quiet but alert, sitting on perch. No faeces seen.
	50	am	Quiet and huddled on perch. Dark faeces.
		pm	Quiet and huddled but alert. No faeces seen.
	51	am	Quiet and huddled but alert. Normal faeces.
		pm	Quiet, sitting on cage floor. No faeces seen.
	52	am	Quiet and huddled. Normal faeces.
		pm	Quiet but alert. No faeces seen.
	53	am	Quiet and huddled, sitting on ladder, moves lethargically when stimulated. Fluid collection abdomen and around face. Loose faeces.
		pm	Quiet but alert and slightly active, moves when stimulated. Normal faeces.
	54	am	Quiet but alert and slightly active, reacts to external stimuli. Dark faeces.
		pm	Quiet but alert, reacts to external stimuli. No faeces seen.
	55	am	Quiet but alert and occasionally active. Normal faeces.
		pm	Very quiet and huddled, visibly shows generalised swelling. No faeces seen.
	56	am	Quiet and huddled on ladder. Tremors, very unsteady but appears bright when stimulated. No faeces seen. Sacrificed for humane reasons.
Y205m	1	am	Quiet and huddled on perch, alert if stimulated. Normal faeces.
		pm	Quiet but alert, sitting on perch.
	2	am	Quiet but alert, sitting on perch. Loose/normal faeces.
		pm	Quiet and huddled on perch, sitting at back of cage. Small amount of faeces seen.
	3	am	Quiet and huddled but alert. Liquid faeces.
		pm	Quiet, sitting hunched continuously on cage floor. Very liquid faeces. Sacrificed for humane reasons.
Y203m	1	am	Lying on cage floor, tries to move and sit up when stimulated, unsteady. Later collapsed on cage floor. Sacrificed for humane reasons.
Y199m	1	am	Quiet but alert. Dry scab. Nasal discharge. Normal faeces.
		pm	Quiet but alert. Slow when moving.. No faeces seen.
	2	am	Quiet but alert, huddled on perch, slow when moving. Normal faeces.
		pm	Quiet but alert, huddled on perch, slow when moving. Normal faeces.
	3	am	Quiet but alert, sitting on perch, not very active.
		pm	Quiet and huddled on perch, reluctant to move.
	4	am	Quiet but alert, huddled in slightly unusual posture. Slightly loose/normal faeces.
		pm	Quiet but alert, lying on cage floor. Appears in discomfort especially when passing urine, with abdominal muscular spasms.
	5	am	Quiet, sitting on cage floor, appears uncomfortable. Normal faeces.
		pm	Quiet, sitting on perch. No faeces seen.
	6	am	Quiet but alert, sitting on cage floor, appears uncomfortable. Good urine output.
		pm	Quiet but alert, sitting on cage floor, appears uncomfortable.
	7	am	Quiet but alert, huddled on cage floor. Vomit in tray. Loose faeces.
		pm	Quiet but alert, huddled on cage floor. Vomit in tray. Loose faeces.

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Individual clinical signs

Animal no./sex	Day no.		Observation
Y199m	8	am	Quiet but alert, huddled on cage floor. Loose faeces.
		pm	Quiet but alert, huddled on cage floor. Loose faeces.
	9	am	Quiet but alert, sitting on cage floor. Normal faeces.
		pm	Quiet and huddled, alert at times.
	10	am	Quiet but alert, sitting in unusual posture on perch. Vomit in tray.
		pm	Quiet but alert, normal posture, moves slowly when stimulated.
	11	am	Quiet but alert, sitting on cage floor.
		pm	Quiet but alert, sitting on cage floor.
	12	am	Quiet, standing on all fours, shows intermittent discomfort.
		pm	Quiet, standing on all fours, shows intermittent discomfort.
	13	am	Quiet and huddled on perch. Vomit in tray. No faeces seen.
		pm	Alert and fairly active.
	14	am	Quiet but alert, huddled on perch.
		pm	Quiet but alert, huddled on perch.
	15	am	Quiet but alert, huddled on perch.
		pm	Quiet but alert, huddled on perch.
	16	am	Quiet but alert, huddled on perch. Normal faeces.
		pm	Quiet but alert, huddled on perch.
	17	am	Quiet but alert, unusual posture on perch.
		pm	Quiet but alert.
	18	am	Quiet but alert.
		pm	Quiet but alert, sitting on perch. No faeces seen.
	19	am	Quiet but alert, occasionally active. Normal faeces..
		pm	Quiet but alert, slightly active. Dark faeces..
	20	am	Alert, sitting on perch. Dark faeces.
		pm	Alert, sitting on perch. No faeces seen.
	21	am	Alert, sitting on perch. Normal faeces.
		pm	Alert, sitting on perch.
	22	am	Quiet but alert.
		pm	Quiet but alert, occasionally active.
	23	am	Quiet but alert.
		pm	Quiet but alert.
	24	am	Quiet and huddled on cage floor, alert and active when stimulated. Dark faeces.
		pm	Records not completed
	25	am	Quiet but alert.
		pm	Alert, occasionally active.
	26	am	Quiet but alert.
		pm	Alert and active.
	27	am	Quiet but alert, fairly active when approached.
		pm	Quiet but alert, slightly active.
	28	am	Alert and active. Loose faeces.
		pm	Quiet but alert. No faeces seen.
	29	am	Alert and active. Normal faeces.
		pm	Alert and active.

APPENDIX 11

Individual clinical signs

Animal no./sex	Day no.		Observation
Y199m (contd)	30	am	Alert and active.
		pm	Alert and active.
	31	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert, sitting on perch.
	32	am	Quiet but alert.
		pm	Quiet but alert.
	33	am	Quiet but alert.
		pm	Quiet but alert. No faeces seen.
	34	am	Quiet but alert, reluctant to move. Normal faeces.
		pm	Quiet but alert, reluctant to move.
	35	am	Quiet but alert, occasionally active.
		pm	Quiet but alert, occasionally active.
	36	am	Quiet but alert, occasionally active.
		pm	Alert and active. No faeces seen.
	37	am	Quiet and huddled on perch, but alert and active when approached. Normal faeces.
		pm	Quiet and huddled.
	38	am	Quiet and huddled, but alert when approached.
		pm	Quiet but alert.
	39	am	Quiet but alert. Bloody urine. Dark/loose faeces.
		pm	Quiet and huddled.
	40	am	Quiet and huddled. Loose faeces.
		pm	Quiet but alert, sitting on perch. Loose faeces.
	41	am	Quiet but alert, leaning on ladder. Loose faeces.
		pm	Records not completed
	42	am	Quiet but alert. Normal faeces
		pm	Quiet and huddled on perch.
	43	am	Quiet but alert.
		pm	Quiet but alert, reluctant to move..
	44	am	Quiet but alert, sitting on perch, reluctant to move..
		pm	Alert and active, sitting on perch. Dark faeces.
	45	am	Quiet and huddled. Normal faeces.
		pm	Quiet and huddled.
	46	am	Quiet but alert, sitting on perch. Dark faeces.
		pm	Quiet but alert. No faeces seen.
	47	am	Very quiet and huddled, appears reluctant to move.
		pm	Very quiet and huddled, moves slowly. Good urine output. Dark faeces.
	48	am	Quiet and huddled, leaning against ladder with eyes shut. Dark loose faeces.
		pm	Quiet but alert. Normal faeces.
	49	am	Quiet and huddled against ladder. Dark faeces.
		pm	Appears alert, vocalising. No faeces seen
	50	am	Very quiet, reluctant to move. Urine output reduced. Loose faeces.
		pm	Sacrificed because of biochemistry findings and condition.
Y207m	1	am	Quiet and huddled, in obvious discomfort, continually lying down. Active when stimulated but reluctant to move.
		pm	Sacrificed for humane reasons.

APPENDIX 11

Individual clinical signs

Animal no./sex	Day no.		Observation
Y202f	1	am	Quiet and huddled at back of cage, reluctant to move. No faeces seen.
		pm	Quiet but alert, huddled on perch, reluctant to move, heavy lidded.
	2	am	Quiet but alert, sitting on perch, reluctant to move. Liquid/loose faeces.
		pm	Quiet, sitting in corner of cage, reluctant to move. No faeces seen.
	3	am	Quiet but alert, not very active. Diarrhoeic.
		pm	Quiet, lying on cage floor. Vomit in tray. Liquid/loose faeces.
	4	am	Quiet but alert, slow movements when stimulated, heavy lidded. Loose faeces.
		pm	Quiet but alert, slow movements when stimulated, heavy lidded. Low urine output. Loose faeces.
	5	am	Quiet, reluctant to move. Still passing no urine. Abdomen swollen. Sacrificed for humane reasons.
Y213m	1	am	Quiet but alert, sitting on perch. Green vomit in tray. No faeces seen.
		pm	Quiet but alert, on perch.
	2	am	Quiet but alert, huddled in corner of cage.
		pm	Quiet but alert.
	3	am	Quiet but alert, sitting on perch. Normal faeces.
		pm	Quiet, slightly subdued but alert, sitting on perch.
	4	am	Quiet but alert, huddled on perch. Dark faeces.
		pm	Quiet but alert. Normal faeces.
	5	am	Quiet but alert.
		pm	Quiet but alert, sitting on perch. Pale loose faeces.
	6	am	Alert, sitting on perch. Pale loose faeces.
		pm	Alert, sitting on perch. No faeces seen.
	7	am	Quiet but alert, sitting on cage floor. Loose faeces.
		pm	Quiet but alert, sitting on cage floor. No faeces seen.
	8	am	Alert, sitting on perch. Loose faeces.
		pm	Quiet but alert, sitting on perch. Loose faeces.
	9	am	Quiet and huddled, some slow movements. Loose faeces.
		pm	Alert and active. No faeces seen.
	10	am	Quiet and huddled but alert. Loose faeces.
		pm	Quiet but alert, sitting on perch resting against ladder. No faeces seen.
	11	am	Quiet but alert. Normal faeces.
		pm	Quiet but alert. Dark faeces.
	12	am	Quiet and huddled. Normal faeces.
		pm	Quiet but alert, sitting on perch, slightly active. No faeces seen.
	13	am	Quiet and huddled but alert. Normal faeces.
		pm	Huddled on perch, but alert.
	14	am	Quiet and huddled but alert, moves when stimulated. Normal faeces.
		pm	Quiet and huddled but alert when stimulated, resting on ladder. No faeces seen.
	15	am	Reluctant to move when stimulated. Loose faeces.
		pm	Quiet but alert, sitting on perch, heavy lidded. Loose faeces.
	16	am	Quiet but alert, sitting on perch. Loose faeces.
		pm	Quiet but alert, sitting on perch. No faeces seen.
	17	am	Quiet but alert, sitting in corner of cage.
		pm	Quiet but alert. No faeces seen.
	18	am	Quiet but alert, sitting on perch. Extremely liquid bloody faeces.
		pm	Collapsed on cage floor. Sacrificed for humane reasons.

APPENDIX 11

Individual clinical signs

Animal no./sex	Day no.		Observation
Y215m	1	am	Quiet but alert if stimulated. Lying on cage floor showing signs of discomfort. Vomit in tray. No faeces seen.
		pm	Quiet but alert if stimulated. Normal faeces.
	2	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert, sitting on perch.
	3	am	Quiet but alert, sitting on cage floor.
		pm	Quiet but alert, sitting on cage floor.
	4	am	Quiet but alert, huddled on cage floor. Vomit in tray.
		pm	Quiet but alert.
	5	am	Quiet, sitting on cage floor.
		pm	Quiet but alert, sitting on perch or cage floor.
	6	am	Quiet but alert, occasionally active. dark loose faeces.
		pm	Quiet but fairly active, sitting on cage floor. No faeces seen.
	7	am	Quiet but alert, sitting on cage floor. Dark faeces.
		pm	Quiet but alert, sitting on cage floor. Vomit in tray. No faeces seen.
	8	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert, occasionally active.
	9	am	Quiet but alert. Scratching at wound. No faeces seen.
		pm	Quiet but alert, sitting on perch. Normal faeces.
	10	am	Alert and active.
		pm	Quiet but alert, sitting on perch leaning against ladder No faeces seen.
	11	am	Alert and active. Normal faeces.
		pm	Quiet but alert, sitting on perch, slightly active. no faeces seen.
	12	am	Quiet but alert. Normal faeces.
		pm	Quiet but alert, slightly active when stimulated. No faeces seen.
	13	am	Quiet but alert and active when stimulated. Normal faeces.
		pm	Quiet and huddled on cage floor.
	14	am	Quiet and huddled but alert, moves when stimulated.
		pm	Quiet and huddled but alert, moves when stimulated.
	15	am	Alert when stimulated.
		pm	Quiet but alert, unusual posture on cage floor
	16	am	Quiet but alert.
		pm	Quiet and huddled, appears slightly subdued. No faeces seen.
	17	am	Quiet but alert.
		pm	Quiet but alert, sitting on cage floor.
	18	am	Quiet but alert, sitting on cage floor. Normal faeces.
		pm	Quiet but alert, sitting on cage floor.
	19	am	Quiet and huddled. Dark faeces.
		pm	Quiet and huddled. Dark faeces.
	20	am	Quiet and slightly huddled but alert. Dark faeces.
		pm	Quiet and huddled but alert. Dark faeces.
	21	am	Quiet and huddled on cage floor, reluctant to move. Dark faeces.
		pm	Quiet and huddled. No faeces seen.
	22	am	Quiet but alert. Normal faeces.
		pm	Quiet but alert, occasionally active for short periods.
	23	am	Quiet but alert, occasionally active. Loose faeces.
		pm	Quiet but alert, occasionally active. No faeces seen.
	24	am	Quiet but alert. Normal faeces.
		pm	Quiet but alert.

APPENDIX 11

Individual clinical signs

Animal no./sex	Day no.		Observation
Y215m (contd)	25	am	Quiet but alert.
		pm	Quiet but alert.
	26	am	Subdued and huddled, reluctant to move, becomes alert when stimulated. Loose faeces.
		pm	Quiet but alert.
	27	am	Quiet, slightly huddled but alert. Normal faeces.
		pm	Quiet but alert. No faeces seen.
	28	am	Quiet and huddled but alert.
		pm	
	29	am	Quiet and huddled, no movement. Loose faeces.
		pm	Quiet but alert, huddled on perch. No faeces seen.
	30	am	Quiet but alert. Loose faeces.
		pm	Quiet but alert. No faeces seen.
	31	am	Very subdued, huddled on perch. Red urine. Loose faeces.
		pm	Quiet and huddled, sitting on cage floor, reacts to external stimulation. Dark faeces.
	32	am	Quiet but alert. Liquid faeces.
		pm	Quiet and huddled. No faeces seen.
	33	am	Quiet but alert, huddled on perch, responds to external stimulation. Normal faeces.
		pm	Quiet but alert.
	34	am	Quiet but alert. Pale faeces.
		pm	Quiet but alert. No faeces seen.
	35	am	Quiet and huddled, lying on ladder, slightly active. Vomit in tray. Normal faeces.
		pm	Quiet but alert. No faeces seen.
	36	am	Quiet and huddled but alert. Normal faeces.
		pm	Quiet, sitting on cage floor. Vomit in tray. Loose faeces.
	37	am	Quiet and huddled. Loose faeces.
		pm	Quiet but alert. Loose faeces.
	38	am	Quiet and huddled on perch, eyes shut. Liquid faeces.
		pm	Quiet but alert, sitting on perch, reluctant to move. No faeces seen.
	39	am	Quiet, sitting on bottom of cage, slightly subdued, reluctant to move. Small vomit in tray. Dark faeces. Later in collapsed state. Sacrificed for humane reasons.

APPENDIX 11

Individual clinical signs

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day, the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1) except where the animal did not survive beyond Day 0.

APPENDIX 11

(Individual clinical signs - continued)

Animal no./sex	Day no.		Observation
Y231m	0	pm	Found dead in transport box.
Y237m	0	pm	Found collapsed, attempted to artificially ventilate, unable to resuscitate, heart stopped.
Y217m	1	am	Quiet and subdued, lying down most of the night, normal faeces, blood/urine passed, green liquid vomit in tray, lying on cage floor, reluctant to move if stimulated. Sacrificed for humane reasons.
Y234f	1	am	Recovered well, quiet but alert, no urine passed, normal faeces.
		pm	Quiet but alert, laying on perch, no faeces.
	2	am	Quiet but alert, occasionally active, reacts to external stimuli, dark faeces.
		pm	Sitting on ladder, and occasionally unsteady, not very active but alert, no faeces.
	3	am	Quiet but alert, occasionally active, dark faeces.
		pm	Quiet but alert, occasionally active, loose and dark faeces.
	4	am	Quiet but alert, reacts to external stimuli, discoloured white mucus in tray, no faeces.
		pm	Quiet but alert, occasionally active, no faeces.
	5	am	Quiet but alert, dark faeces.
		pm	Quiet but alert, sitting on cage floor, scratching at wound, occasionally active, very liquid faeces passed while being dosed.
	6	am	Quiet but alert, active if stimulated, pale loose faeces.
		pm	Alert and fairly active, pale loose faeces.
	7	am	Alert and active, loose faeces.
		pm	Quiet but alert, active if stimulated, vomit in tray, normal faeces.
	8	am	Alert and active, vocalising, pale loose faeces. (blood in loose faeces)
		pm	Alert and active, blood stained loose faeces.
	9	am	Alert and active, picking at wound, vomit in tray, normal faeces.
		pm	Alert and active.
	10	am	Alert, occasionally active, loose faeces.
		pm	Quiet but alert, slightly loose faeces.
	11	am	Quiet but alert, normal faeces, urine output satisfactory.
		pm	Alert and active, no faeces.
	12	am	Quiet, sitting on cage floor, loose nearly liquid faeces.
		pm	Quiet but alert, sitting in hammock, loose faeces.
	13	am	Quiet but alert, occasionally active if stimulated, pale loose faeces.
		pm	Quiet but alert, huddled at back of cage, reluctant to move, pale loose faeces, (vomit in tray and urine collection bottle).
	14	am	Alert and active, normal faeces.
		pm	Alert and active, dark faeces.
	15	am	Quiet but alert, occasionally active, dark faeces.
		pm	Quiet but alert, huddled at back of cage, observed vomiting, dark faeces.

( ) Noted on dose record sheet

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day No.		Observation
Y234f (cont)	16	am	Alert and active, moving around cage, normal faeces.
		pm	Alert, sitting on ladder, reacts to external stimuli, vomited, dark faeces.
	17	am	Alert, sitting on ladder, reacts to external stimuli, normal faeces.
		pm	Quiet but alert, sitting on perch, reacts to external stimuli (vomit on cage floor/drip bucket).
	18	am	Quiet but alert, sitting on perch, reacts to external stimuli, very loose faeces.
		pm	Quiet but alert, standing on perch holding onto cage, liquid faeces.
	19	am	Alert and fairly active, vomited, liquid faeces
		pm	Quiet but alert, moves when stimulated, dark faeces
	20	am	Alert and fairly active, loose faeces.
		pm	Alert and fairly active, normal faeces.
	21	am	Alert and active, vomit in tray.
		pm	Quiet but alert, occasionally active.
	22	am	Alert and active, loose faeces.
		pm	Alert and active, no faeces.
	23	am	Alert and active, loose faeces.
		pm	Quiet but alert, occasionally active, white vomit in tray, normal faeces.
	24	am	Alert and fairly active, white vomit in tray.
		pm	Alert and active.
	25	am	Quiet but alert, slightly active, very loose faeces.
		pm	Alert and active, sitting on ladder, no faeces.
	26	am	Alert and active, quiet at times, loose faeces.
		pm	Alert, occasionally active, dark soft faeces.
	27	am	Alert and active, loose dark faeces.
		pm	Alert and slightly active, no faeces.
	28	am	Alert and active, occasionally quiet, loose faeces, (retch post-dose)
		pm	Alert and active, occasionally quiet, loose faeces
	29	am	Quiet but alert, loose faeces.
		pm	Quiet but alert, occasionally active, vomited, no faeces. Later, active when stimulated, fluid collecting around lower abdomen and thighs, liquid faeces.
	30	am	Quiet but alert, slightly active, sitting on ladder, oedema in legs and perineum unchanged, loose faeces, (retch post-dose).
		pm	Quiet but alert, moves slowly if stimulated, no faeces. Later, quiet and huddled over ladder with head down, minimal interest shown when stimulated, vomit in tray, no faeces. Rapid deterioration, collapsed on cage floor. Sacrificed for humane reasons.
Y235m	0	pm	Kidney not viable, animal sacrificed under anaesthesia in theatre.

( ) Noted on dose record sheet

APPENDIX 11

Individual clinical signs

Explanatory notes

1. Only first and last observations of the working day are reported. Due to manipulations/investigations performed on animals during the day, the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1).

APPENDIX 11

(Individual clinical signs – continued)

Animal no./sex	Day no.		Observation
Y233m	1	am	Quiet but alert, very liquid vomit in cage.
		pm	Quiet and subdued, reluctant to move, eyes shut but responds to external stimuli.
	2	am	Huddled, lying on bottom of cage, reacts to external stimuli, occasionally moving around cage.
		pm	Quiet but alert, unusual posture.
	3	am	Quiet but alert, sitting on perch, some reaction to external stimuli, vomit in cage.
		pm	Quiet but alert, sitting on perch.
	4	am	Quiet but alert, active when approached, dark faeces. Subdued and huddled, reluctant to move, appears weak and unsteady, limb tremors and dark faeces noted prior to sacrifice. Sacrificed for humane reasons.
Y239m	1	am	Quiet and huddled, eyes closed, loose faeces.
		pm	Alert and active, vomit in cage, sitting on ladder, responds to external stimuli.
	2	am	Alert but quiet, lying against perch, reacts to external stimuli.
		pm	Appears to be in discomfort/ clinging to front of cage, head back, no response to external stimuli, shallow breathing/slow respiration rate, weak, salivating, enlarged abdomen, discoloured gums. Sacrificed for humane reasons.
Y210f	1	am	Quiet but alert, unsteady when moving.
		pm	Quiet but alert, slightly subdued, profuse salivation.
	2	am	Quiet but alert, sitting on ladder.
		pm	Quiet but alert, moves when stimulated.
	3	am	Quiet but alert, active when approached.
		pm	Quiet but alert, reluctant to move.
	4	am	Quiet but alert, sitting on ladder, occasionally active, dark faeces.
		pm	Alert and fairly active, normal faeces
	5	am	Quiet but alert, reacts to external stimuli.
		pm	Alert and active.
	6	am	Quiet but alert, active when disturbed
		pm	Quiet but alert, sitting on ladder, vocalising.
	7	am	Quiet, huddled on ladder, pelleted faeces.
		pm	Collapsed on cage floor, appears weak and unable to get up, breathing shallow and rapid, salivating, heavy lidded eyes, body and limb tremors. Sacrificed for humane reasons.
Y236f	1	am	Quiet but alert, slow movements.
		pm	Subdued and huddled, reluctant to move, slightly unsteady.
	2	am	Quiet but alert, sitting on ladder.
		pm	Sacrificed for humane reasons.

APPENDIX 11

(Individual clinical signs – continued)

Animal no./sex	Day no.		Observation
Y228f	1	am	Quiet but alert.
		pm	Quiet but alert, sitting on ladder, moves when stimulated, pelleted faeces.
	2	am	Quiet but alert and slightly active, normal faeces.
		pm	Quiet but alert, dark faeces.
	3	am	Quiet but alert, occasionally active, normal faeces.
		pm	Subdued, sitting on perch, becomes alert when stimulated but reluctant to move
	4	am	Quiet and huddled on ladder, alert when stimulated but reluctant to move.
		pm	Quiet and huddled on ladder, reluctant to move. Sacrificed for humane reasons.
Y229m	1	am	Alert and active.
		pm	Quiet but alert, sitting on ladder, reluctant to move, unusual posture, swelling around groin.
	2	am	Alert, slightly active, lethargic, sitting on ladder and leaning against cage front, vomit in cage.
		pm	Quiet but alert.
	3	am	Quiet but alert, reluctant to move, dark pelleted faeces.
		pm	Quiet but alert, moves when stimulated, scratching at wound.
	4	am	Quiet but alert, reluctant to move, overnight vomit, dark faeces.
		pm	Quiet, reluctant to move.
	5	am	Quiet but alert, reluctant to move, sitting on ladder with right leg raised off the floor, dark faeces.
		pm	Quiet but alert, occasionally active, picking at wound, huddled on ladder.
	6	am	Quiet but alert, sitting on ladder, normal faeces.
		pm	Sacrificed for humane reasons.

APPENDIX 11

Individual clinical signs

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day, the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1).

APPENDIX 11

(Individual clinical signs - continued)

Animal no./sex	Day no.		Observation
Y240m	1	am	Alert, sitting on perch, normal faeces
		pm	Quiet but alert, occasionally active, later; alert, but reluctant to move.
	2	am	Quiet and huddled, alert when stimulated, normal faeces.
		pm	Alert, sitting on perch.
	3	am	Quiet and huddled on ladder, alert if approached, occasionally active, later quiet and huddled against ladder, alert but reluctant to move, slightly unusual posture
		pm	Alert and reasonably active, no faeces, later quiet but alert when stimulated, laying on ladder.
	4	am	Quiet but alert, active when stimulated, pelleted faeces
		pm	Quiet but alert, sitting on cage floor.
	5	am	Quiet but alert, occasionally active, dark faeces
		pm	Quiet but alert, occasionally active, moves if stimulated but reluctant to move.
	6	am	Quiet but alert, lying across ladder, pelleted faeces
		pm	Quiet but alert, sitting on perch, scratching at wound, dark pelleted faeces
	7	am	Quiet but alert and occasionally active, dark faeces
		pm	Quiet but alert.
	8	am	Quiet and huddled, active when stimulated, loose faeces
		pm	Very quiet and huddled in corner of cage. Little response to external stimulation, generally in poor condition, loose faeces. Sacrificed for humane reasons.
Y241m	1	am	Quiet but alert, sitting on perch, reluctant to move, loose faeces.
		pm	Quiet but alert, huddled against ladder, reluctant to move, vomit in tray.
	2	am	Quiet, alert at times, little response to stimulation, normal faeces.
		pm	Quiet but alert.
	3	am	Quiet but alert, occasionally active, later alert, vocalising, active in cage.
		pm	Quiet and huddled in corner of cage, responds to stimuli but reluctant to move, condition improved later.
	4	am	Laying on cage floor, alert when stimulated, later quiet on perch or lying across ladder, little movement or response to stimulation.
		pm	Quiet, laying across ladder, no response to external stimulation, no movement. Sacrificed for humane reasons.
Y230m	1	am	Quiet but alert.
		pm	Sitting on perch.
	2	am	Quiet but alert when approached, scratching at wound, dark faeces, later huddled on cage floor, alert when approached.
		pm	Quiet but alert, often active, scratching at wound.

APPENDIX 11

(Individual clinical signs - continued)

Animal no./sex	Day no.		Observation
Y230m (cont)	3	am	Quiet but alert, sitting on ladder. Normal faeces.
		pm	Quiet but alert, perched on ladder
	4	am	Quiet but alert, often active, dark faeces
		pm	Quiet but alert sitting on ladder, moves if stimulated.
	5	am	Quiet but alert, sitting on cage floor, dark faeces.
		pm	Alert, sitting on cage floor, normal faeces.
	6	am	Alert and fairly active, loose and pelleted faeces.
		pm	Quiet but alert, sitting on ladder, loose faeces.
	7	am	Quiet, huddled around ladder, reluctant to move, pelleted faeces.
		pm	Quiet, sitting on perch, active when stimulated, dark pelleted faeces.
	8	am	Alert and active, sitting on cage floor, loose faeces.
		pm	Alert, sitting on cage floor, loose/liquid faeces.
	9	am	Alert and active, sitting on perch, picking at scar, loose dark faeces.
		pm	Alert but huddled on cage floor, loose faeces.
	10	am	Quiet but alert, sitting on perch, loose/liquid faeces.
		pm	Alert, sitting on perch, but reluctant to move, normal faeces.
	11	am	Quiet but alert, grooming, loose faeces.
		pm	Quieter than seen earlier, loose/liquid faeces.
	12	am	Alert and active, sitting on ladder, grooming, loose/soft faeces.
		pm	Quiet but alert, loose faeces,.
	13	am	Alert and active, very loose faeces, white froth (vomit) in tray.
		pm	Alert and active, loose faeces.
	14	am	Quiet but alert, huddled on ladder, diet vomit on tray, loose faeces.
		pm	Very subdued and huddled on ladder, eyes closed, body and limb tremors, occasionally scratching at wound, loose faeces. Sacrificed for humane reasons.
Y238f	1	am	General condition improved, alert, occasionally active.
		pm	Subdued, sitting on perch, later collapsed on cage floor, heavy laboured breathing, pale gums, eyes closed, later laying on ladder, laboured breathing, reluctant to move. Subsequently crouching on perch, reluctant to move, no response to handling, all movement passive, appears very weak. Sacrificed for humane reasons.
Y45m	1	am	Quiet and huddled, sitting on perch.
		pm	Quiet and huddled on perch, appears drowsy and heavy lidded, reluctant to move if stimulated, later very unsteady on return to cage, severe limb tremors when moving.
	2	am	Quiet but alert, responds to external stimuli, huddled on perch.
		pm	Alert but not very active, sitting on perch.

APPENDIX 11

(Individual clinical signs - continued)

Animal no./sex	Day no.		Observation
Y45m (cont)	3	am	Quiet but alert, sitting on ladder, active when stimulated, moving around cage, normal faeces
		pm	Quiet but alert, sitting on ladder.
	4	am	Alert and active, pelleted faeces.
		pm	Alert and active, dark faeces
	5	am	Alert and active, moving around cage, dark faeces.
		pm	Alert, sitting on perch, occasionally active, dark faeces.
	6	am	Alert and active, normal faeces.
		pm	Sitting on perch.
	7	am	Alert and active.
		pm	Quieter than noted previously.
	8	am	Alert and active, dark pelleted faeces.
		pm	Quiet and huddled but alert if approached, dark pelleted faeces
	9	am	Alert and active, dark pelleted faeces
		pm	Quiet but alert, normal faeces.
	10	am	Alert and active, dark pelleted faeces.
		pm	Quiet but alert, occasionally active, dark pelleted faeces
	11	am	Alert and active, dark faeces
		pm	Alert, sitting on ladder, dark faeces
	12	am	Alert and active, normal faeces.
		pm	Alert, occasionally active, sitting on ladder, pale soft faeces
	13	am	Alert and active, normal faeces
		pm	Alert, sitting on cage floor, occasionally active, pale faeces
	14	am	Alert and active, normal faeces.
		pm	Alert and active.
	15	am	Alert and active, dark faeces.
		pm	Alert, occasionally active.
	16	am	Alert and active, occasionally quiet, scratching abdomen, dark faeces.
		pm	Alert and active if approached, vocalising with surrounding animals, dark faeces.
	17	am	Alert, occasionally active, dark pelleted faeces.
		pm	Quiet but alert, laying on ladder, appears uncomfortable, active when approached, dark pelleted faeces, later alert and active.
	18	am	Alert, sitting on ladder, occasionally active and vocalising, slight bruising on left side of chest, pelleted faeces.
		pm	Quiet and huddled, noticeably quieter than earlier, will move if stimulated, increased petechiation and bruising on chest and under arms, pelleted faeces.

APPENDIX 11

(Individual clinical signs - continued)

Animal no./sex	Day no.		Observation
Y45m (cont)	19	am	Alert, sitting on ladder, occasionally active, reduction in bruising, pelleted faeces
		pm	Alert, sitting on perch, occasionally active.
	20	am	Alert, occasionally active and vocalising, dark pelleted faeces.
		pm	Quiet but alert, sitting on ladder, normal faeces
	21	am	Quiet but alert, sitting on perch, sometimes active
		pm	Alert, sitting on perch, occasionally active
	22	am	Quiet but alert, shaking periodically
		pm	Bright and alert, occasionally active
	23	am	Quiet but alert, frequently lying on ladder but moves when approached
		pm	Quiet but alert.
	24	am	Quiet but alert, occasionally active, dark pelleted faeces.
		pm	Sacrificed for humane reasons.
Y128f	1	am	Quiet but alert, sitting on top of ladder.
		pm	Alert, sitting upright on ladder, normal faeces
	2	am	Alert, standing upright on ladder.
		pm	Alert and active.
	3	am	Alert, sitting on ladder, occasionally active.
		pm	Alert, sitting on top of ladder, active when stimulated.
	4	am	Alert and active, sitting on top of ladder.
		pm	Alert, sitting on ladder.
	5	am	Quiet but alert, sitting on ladder.
		pm	Alert, occasionally active.
	6	am	Quiet but alert, sitting on ladder.
		pm	Alert, resting on ladder.
	7	am	Alert and active.
		pm	Quieter than morning but alert, dark faeces.
	8	am	Alert and active, loose faeces.
		pm	Quiet and huddled on perch, eyes closed.
	9	am	Alert and active, liquid faeces.
		pm	Quiet, huddled, vomit in tray, liquid faeces.
	10	am	Quiet and huddled on ladder, alert if stimulated, vomit in tray, loose/liquid faeces
		pm	Quiet and huddled on ladder, piloerection, occasionally alert but only if stimulated, green loose liquid faeces. Sacrificed for humane reasons.
Y49m	1	am	Generally quiet but bright.
		pm	Quiet but alert.
	2	am	Alert and reasonably active.
		pm	Alert and fairly active.
	3	am	Alert, maintaining unusual posture.
		pm	Alert and active, appears to be uncomfortable.

APPENDIX 11

(Individual clinical signs - continued)

Animal no./sex	Day no.		Observation
Y49m (cont)	4	am	Alert and active, occasionally adopts an unusual posture, bruising around penis and scrotal oedema, scratching abdomen, dark faeces .
		pm	Quiet but alert, sitting on ladder, moves if stimulated.
	5	am	Bright and alert and occasionally active, scratching wound.
		pm	Quiet but alert, huddled while leaning against ladder.
	6	am	Subdued and huddled, becomes alert if stimulated but reluctant to move, dark pelleted faeces.
		pm	Quiet and huddled, lying on ladder, alert if stimulated, reluctant to move, loose faeces.
	7	am	Lying on cage floor, little reaction to external stimuli, later collapsed on cage floor. Sacrificed for humane reasons.
Y172f	1	am	Quiet, very little activity, appears bright when stimulated, possible vomit in tray.
		pm	Quiet but alert, active at times.
	2	am	Quiet but alert, moves when stimulated, rasping breathing.
		pm	Sitting on ladder but alert, rasping breathing very noticeable.
	3	am	Quiet but alert, active when stimulated, respiratory noise much reduced, loose faeces.
		pm	Quiet but alert, sitting on ladder, vomit in tray, loose faeces.
	4	am	Quiet but alert, sitting on ladder, breathing improved, vomit in tray, loose faeces.
		pm	Quiet but alert, sitting on ladder, occasionally huddled, loose faeces.
	5	am	Quiet but alert, sitting on perch, appears weak when moving around cage, dark loose faeces.
		pm	Bright and alert, dark loose and soft faeces.
	6	am	Quiet but alert, sitting on ladder, abdomen appears slightly swollen, vomit in tray, dark loose faeces.
		pm	Quiet and huddled but alert if stimulated, occasionally active, looking very weak, soft and loose faeces.
	7	am	Quiet but alert, occasionally active and vocalising, loose faeces.
		pm	Quiet but alert, more active than earlier, soft faeces. Subsequently quiet and huddled, alert when stimulated, sometimes crouched on cage floor and appears to be straining, later quiet but alert, sitting on ladder.
	8	am	Quiet but alert, occasionally subdued and huddled, slight limb tremors particularly when moving, abdomen slightly swollen, loose faeces. Very quiet, low urine output. Sacrificed for humane reasons.

APPENDIX 11

Individual clinical signs

Explanatory notes

1. Only first and last observations of the working day are reported. Due to manipulations/investigations performed on animals during the day, the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1).

APPENDIX 11

(Clinical signs - continued)

Animal No./sex	Day no.		Observation
A4f	1	am	Quiet and lying on cage floor, responsive and alert when simulated and rises on all fours.
		pm	Sitting on ladder, quiet though alert when stimulated, eyes heavy-lidded.
	2	am	Quiet but alert when disturbed, sitting on perch.
		pm	Quiet but alert, sitting on ladder, interested in surroundings.
	3	am	Alert.
		pm	Quiet but alert, occasionally active.
	4	am	Quiet but alert, occasionally active. Dark faeces.
		pm	Alert and active, sitting on ladder. Normal faeces.
	5	am	Quiet at times, alert. Dark faeces.
		pm	Alert, sitting on ladder. Normal faeces.
	6	am	Alert and active.
		pm	Quiet but alert, sitting on ladder grooming pairing partner.
	7	am	Alert when stimulated and active. Vomit in tray. Sacrificed for humane reasons.
A7m	1	am	Bright and alert, sitting on ladder. Adopts threatening posture if approached.
		pm	Quiet but alert, sitting on perch, occasional activity.
	2	am	Quiet but alert, active when stimulated. Vomit in tray.
		pm	Quiet but alert, sitting on cage floor grooming.
	3	am	Quiet but alert, sitting on ladder, becomes aggressive when approached.
		pm	Quiet but alert, sitting on ladder, active and aggressive when stimulated.
	4	am	Quiet but alert, sitting on perch, reacts to external stimuli. Dark faeces.
		pm	Alert and fairly active. Dark faeces.
	5	am	Quiet but alert, sitting on ladder, mildly aggressive when approached. Dark faeces.
		pm	Alert, occasional activity. Dark faeces.
	6	am	Quiet but alert, sitting on ladder. Dark faeces.
		pm	Quiet but alert, some activity. Dark faeces.
	7	am	Quiet but alert, sitting on ladder. Normal faeces.
		pm	Quiet, huddled posture, general lack of movement, not responsive. Sacrificed for humane reasons.
A6f	1	am	Very quiet, reluctant to move, eyes generally closed.
		pm	Very quiet and subdued, sitting on ladder, eyes closed, reluctant to move.
	2	am	Very quiet, reluctant to move, eyes generally closed.
		pm	Sacrificed for humane reasons.
A10f	1	am	Quiet but alert.
		pm	Huddled on ladder, little movement, eyes appear heavy/closing.
	2	am	Quiet but alert.
		pm	Quiet but alert, sitting on ladder with head down, moves when stimulated.
	3	am	Collapsed after blood sampling, very weak when handled, faint pulse, prior to handling the animal was quiet but alert, though reluctant to move. Sacrificed for humane reasons.

APPENDIX 11

Individual clinical signs

Explanatory notes

Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day, the signs are considered to be unrepresentative of the underlying condition of each animal.

Clinical signs are reported from the day following transplant (Day 1) except where the animal did not survive beyond Day 0.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y150F	1	am	Quiet but alert, slow movements around cage.
		pm	Very alert and active, moving around cage.
	2	am	Quiet but alert.
		pm	Quiet but alert, sitting on ladder, occasionally active.
	3	am	Quiet but alert, vomit in tray, redness and scabbing on area surrounding wound (probably due to scratching).
		pm	Alert, sometimes active, sitting on ladder.
	4	am	Quiet but alert, sitting on ladder, moves when stimulated, redness and dry scabbing on abdomen, probably due to scratching, dark faeces.
		pm	Quiet but alert, picking at wound, redness and dry scabbing on abdomen around wound, probably due to scratching, dark pelleted faeces. Later; scratch near wound weeping serum and a small amount of blood observed.
	5	am	Quiet but alert, scratching wound, normal faeces.
		pm	Quiet but alert, sometimes active when stimulated, sitting on ladder.
	6	am	Quiet but alert, pelleted faeces.
		pm	Quiet but alert, active, sitting on ladder, scratching stomach area, pelleted faeces.
	7	am	Quiet but alert, normal faeces.
		pm	Quiet but alert, sitting on ladder.
	8	am	Quiet but alert, standing on ladder, hanging from roof of cage, dark faeces.
		pm	Quiet and huddled, piloerection, responds a little to mild stimulation. Later; observed salivating following vomiting, appears quiet.
	9	am	Alert when stimulated, generally quiet and huddled, dark pelleted faeces.
		pm	Alert and active.
	10	am	Alert and active, normal faeces.
		pm	Quiet but alert.
	11	am	Alert and occasionally active.
		pm	Alert and occasionally active.
	12	am	Quiet but alert and active, sitting on ladder.
		pm	Quiet but alert and active, sitting on ladder.
	13	am	Alert and reasonably active, sitting on ladder.
		pm	Quiet but alert, sitting on ladder, moves when stimulated, red stained urine, dark faeces.
	14	am	Alert, responds to external stimuli, sitting on top of ladder, dark faeces.
		pm	Alert and active, grooming pairing partner, dark faeces.
	15	am	Alert and responsive, sitting on ladder, sometimes quiet, normal faeces
		pm	Quiet but alert, active.
	16	am	Quiet but alert, active when stimulated.
		pm	Quiet but alert, active when stimulated.
	17	am	Quiet but alert, occasionally active when stimulated, dark faeces. Large vomit following dose.
		pm	Alert and active.
	18	am	Alert and active, dark faeces.
		pm	Alert, sitting quietly on perch, gentle activity, salivating following dose.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y150F (contd)	19	am	Alert and active, dark faeces. Vomited during dosing.
		pm	Alert and active, normal faeces.
	20	am	Alert and active, vocalising, pale faeces.
		pm	Quiet but alert, occasionally active.
	21	am	Alert and fairly active, dark faeces.
		pm	Quiet but alert, sitting on ladder.
	22	am	Alert and active, dark faeces, vomit on hammock.
		pm	Quiet but alert, occasionally active, vomit on hammock.
	23	am	Quiet but alert, active when disturbed.
		pm	Quiet but alert, occasionally active.
	24	am	Alert and fairly active, dark faeces.
		pm	Alert and active, normal faeces.
	25	am	Alert and active, dark faeces, vomit in tray, dark faeces.
		pm	Quiet and alert, sitting on hammock, occasional activity, dark loose faeces.
	26	am	Alert and active, dark loose faeces.
		pm	Alert and active, gentle activity, dark faeces.
	27	am	Quiet but alert, active when approached, normal faeces.
		pm	Quiet but alert, active when approached.
	28	am	Quiet and huddled, appears alert when stimulated.
		pm	Alert, occasionally active, vocalising.
	29	am	Quiet but alert, sometimes active, sitting huddled in hammock.
		pm	Quiet but alert, grooming pairing partner.
	30	am	Quiet but alert, sitting on perch, huddled.
		pm	Quiet but alert, becoming active when stimulated.
	31	am	Alert and active, occasionally huddled on ladder, dark faeces.
		pm	Quiet, sitting in hammock, alert when stimulated.
	32	am	Quiet but alert, sitting on ladder, occasionally active, dark faeces.
		pm	Alert, gentle activity, dark faeces.
	33	am	Quiet but alert, sitting on ladder.
		pm	Bright and alert, gentle activity, dark faeces.
	34	am	Quiet but alert, occasionally active, dark faeces.
		pm	Alert, fairly active, dark faeces. Later; vomit in tray.
	35	am	Quiet and huddled on hammock, occasionally active, dark faeces, vomit in tray. Later; abdomen appears swollen and distended.
		pm	Quiet and huddled on hammock/ladder, responds to external stimuli, reluctant to move, loose faeces.
	36	am	Quiet but alert, sitting in hammock, grooming self, abdomen appears swollen and distended, loose/liquid faeces.
		pm	Quiet but alert when stimulated, liquid faeces
	37	am	Quiet but alert, sitting in hammock, grooming self, loose faeces
		pm	Quiet but alert, sitting in hammock, loose/liquid faeces, abdomen appears distended, swelling around both eyes.
	38	am	Quiet but alert, sitting in hammock, loose/liquid faeces
		pm	Quiet but alert, loose/liquid faeces

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y150F (contd)	39	am	Quiet and huddled in hammock, appears alert, loose/liquid faeces.
		pm	Alert, reluctant to move, loose faeces, vomit in tray.
	40	am	Quiet but alert, loose faeces.
		pm	Quiet but alert.
	41	am	Quiet but alert, sitting on perch, loose faeces.
		pm	Sacrificed for humane reasons.
Y225F	1	am	Quiet but alert, lying of ladder, sits up when stimulated, vomiting clear yellow fluid.
		pm	Quiet and huddled on ladder, reluctant to move even when stimulated.
	2	am	Quiet but alert, pelleted faeces.
		pm	Quiet but alert, appears tender, observed straining to urinate, sitting on perch. Later; observed vomiting clear yellow fluid.
	3	am	Quiet but alert, sitting on ladder, occasionally huddled, reluctant to move when stimulated.
		pm	Quiet and huddled, sitting on ladder, becomes alert when stimulated but quickly returns to huddled posture, observed straining to urinate.
	4	am	Quiet but alert, sitting on ladder, [alert and playing but hunched and immobile].
		pm	Sitting on perch .
	5	am	Quiet but alert.
		pm	Quiet but alert, sitting on ladder, appears to be straining.
	6	am	Quiet but alert, huddled on ladder.
		pm	Quiet but alert, huddled on ladder.
	7	am	Quiet but alert, leaning across ladder, appears to be straining to urinate.
		pm	Quiet but alert, leaning across ladder, appears to be straining to urinate.
	8	am	Appears subdued and huddled on ladder, fairly alert when stimulated, reluctant to move, dark faeces. Later; very subdued and unsteady, vacant expression and disinterested in surroundings, abdomen distended.
		pm	Sedated; struggling to breathe whilst sedated, yellow fluid draining from nostrils. Sacrificed for humane reasons
Y148F	1	am	Lying on cage floor, little reaction to stimuli, sits up when disturbed. Later; lying on cage floor, eyes closed, not reacting to stimuli. Sacrificed for humane reasons
Y256M	1	am	Quiet, lying on cage floor, becomes fairly alert and sits up when stimulated, red staining around penis and scrotal area.
		pm	Sitting on perch, resting against front of cage, becomes alert for short periods when stimulated but quickly returns to original posture. Dried blood around penis and scrotum, dark pelleted faeces.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y256F (contd)	2	am	Sitting on cage floor, resting against cage front, appears asleep, becomes alert for short periods when stimulated but quickly returns to original posture, vomit in tray.
		pm	Quiet but alert, sitting on perch.
	3	am	Sitting on perch, leaning on front of cage, appears aware and alert when stimulated. Later; vomited following dose, animal appears very subdued.
		pm	Subdued and huddled in corner of cage, alert when stimulated but reluctant to move.
	4	am	Very quiet, sometimes alert when stimulated, sitting in cage floor. Later; observed vomiting.
		pm	Very subdued and huddled, not responding to stimuli, continually salivating. Sacrificed for humane reasons.
Y254M	0	am	Died in theatre.
Y245M	0	am	No abnormalities detected, large amount of vomit seen in tray, sacrificed during surgery due to donor kidneys being poorly perfused.
Y251M	1	am	Quiet but alert when stimulated, lying on ladder, observed straining to urinate, appears slightly heavy lidded, heavy bruising on left arm.
		pm	Quiet but alert, sitting upright.
	2	am	Very quiet, lying across ladder, alert and aware of surroundings, possible remnants of old vomit seen in tray, scratches on abdomen (right side of wound).
		pm	Alert, looking around, sitting quietly on perch.
	3	am	Lying down, reluctant to move even when stimulated, appears alert.
		pm	Lying on cage floor, slowly sits up when stimulated, straining to urinate. Later; sitting on cage floor in a huddled posture, looking alert. After dose quiet but alert, sitting on ladder, huddled.
	4	am	Quiet and huddled, lying on ladder, aware of surroundings but reluctant to move even when approached, dark faeces.
		pm	Quiet and huddled on ladder, responds to external stimuli.
	5	am	Quiet but alert, sitting on perch, occasionally active, very dark soft faeces.
		pm	Quiet but alert, sitting on perch.
	6	am	Quiet but alert, sitting on ladder, appears to be straining to urinate, kidney appears large, some scratch marks on abdomen near kidney site, dark soft faeces.
		pm	Quiet but alert, sitting on ladder, dark faeces.
	7	am	Quiet but alert, often seen lying down, vomit in cage, straining to urinate.
		pm	Quiet but alert, sitting on perch, dark faeces. Sacrificed for humane reasons.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y257M	1	am	Quiet but alert.
		pm	Quiet but alert, occasionally active, dark faeces. Later, alert, gentle activity.
	2	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert, active when stimulated, dark faeces.
	3	am	Quiet but alert, slightly active, responds well to external stimuli, dark faeces.
		pm	Quiet but alert, sitting on top of ladder, appears to be straining to urinate.
	4	am	Alert and active, appears to be straining to urinate, dark faeces.
		pm	Alert and active, straining to urinate, dark faeces.
	5	am	Quiet but alert, normal faeces.
		pm	Quiet but alert, periodically seen straining to urinate.
	6	am	Quiet but alert, occasional movements, dark faeces, straining to urinate.
		pm	Alert and active, picking at wound, vocalising, dark pelleted faeces straining to urinate.
	7	am	Quiet but alert, sometimes active, sitting on ladder, normal faeces.
		pm	Quiet but alert, occasionally active.
	8	am	Quiet but alert, sitting on ladder, huddled.
		pm	Animal observed vomiting. Quiet but alert, occasionally active.
	9	am	Quiet but alert, lying on ladder, active when stimulated, soft/liquid faeces.
		pm	Quiet but alert, sitting on perch, dark faeces.
	10	am	Quiet but alert, sitting on ladder, dark liquid faeces, vomit in tray.
		pm	Quiet but alert, sitting on ladder. Later, bright, alert and active, dark faeces.
	11	am	Quiet but alert, sitting on perch, dark faeces.
		pm	Quiet and huddled on ladder, alert when stimulated, gentle activity.
	12	am	Alert and fairly active, loose faeces.
		pm	Quiet but alert, occasionally active, loose faeces.
	13	am	Alert and active, normal faeces.
		pm	Alert, less active than morning.
	14	am	Alert and active, moving around cage, vocalising when approached, dark faeces.
		pm	Quiet but alert, occasionally active.
	15	am	Alert and active, loose faeces.
		pm	Very alert, occasionally active, scrotum appears swollen, pale loose faeces.
	16	am	Alert, fairly active, dark faeces.
		pm	Quiet but alert, occasionally active, dark faeces.
	17	am	Quiet but alert, occasionally active, normal faeces.
		pm	Quiet but alert, reluctant to move.
	18	am	Alert and fairly active, pale faeces.
		Pm	Quiet but alert, active, sitting on perch.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y257M (contd)	19	am	Alert, sometimes active, slightly loose faeces.
		pm	Alert, gentle activity, more active when approached, dark faeces.
	20	am	No comment recorded.
		pm	Quiet, sitting on perch, active when approached.
	21	am	Alert and active, normal faeces, straining to urinate.
		pm	Alert and active.
	22	am	Alert and fairly active, dark faeces.
		pm	Quiet but alert, active at times, straining to urinate, looks uncomfortable.
	23	am	Alert, sitting on perch, active when stimulated, normal faeces.
		pm	Alert, active when approached.
	24	am	Alert and fairly active. Later; observed vomiting.
		pm	Quiet but alert.
	25	am	Quiet but alert, sitting on perch, slightly active, vomit in tray.
		pm	Quiet but alert, sitting on ladder. Sacrificed for humane reasons.
Y249M	1	am	Lying on cage floor, active when approached.
		pm	Lying on cage floor, alert when stimulated. Later, alert, occasional gentle activity, generally lying down on back or side on cage floor.
	2	am	Quiet but alert, sitting on perch, active when stimulated.
		pm	Quiet but alert, sitting on perch at front of cage.
	3	am	Quiet but alert, sitting on floor of cage, slightly active when stimulated.
		pm	Alert, gentle activity.
	4	am	Alert and active, dark faeces.
		pm	Alert and active, lying in hammock, dark faeces.
	5	am	Quiet but alert, active, dark faeces.
		pm	Quiet but alert, dark faeces, periodically seen straining to urinate, scratch marks around wound.
	6	am	Quiet but alert, normal faeces. Later; quiet and huddled, sitting on perch, becomes alert when stimulated.
		pm	Quiet, occasional movement, sitting on ladder.
	7	am	Quiet but alert, sitting on perch, leaning on ladder. Later; vomited following dosing.
		pm	Lying on cage floor, reluctant to respond to stimulation, eyes appear sunken, abdomen appears distended. Sacrificed for humane reasons.
Y258M	1	am	Generally quiet.
		pm	Lying on cage floor. Later alert, gentle activity, occasionally leaves perch and crouches on cage floor, vomit on mesh.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y258M (contd)	2	am	Quiet but alert, sitting on perch, active when stimulated, yellow coloured vomit in tray.
		pm	Quiet but alert, sitting on perch at front of cage, active when stimulated.
	3	am	Quiet but alert, sitting in hammock, slightly active, trying to find comfortable position, vomit in tray.
		pm	Sitting in hammock, reacts to external stimuli. Later, alert, gentle activity.
	4	am	Alert and active, dark faeces.
		pm	Alert and active, sitting on perch, moving around to find comfortable position.
	5	am	Alert, dark faeces, liquid vomit in tray.
		pm	Quiet but alert, occasionally huddled, periodically seen straining to urinate.
	6	am	Quiet but alert, dark faeces. Later; quiet but alert, gentle activity when stimulated, observed vomiting liquid.
		pm	Alert and occasionally active, vocalising, vomited on return to cage after dosing.
	7	am	Quiet but alert, active, normal faeces.
		pm	Quiet and lying in unusual posture on ladder, reluctant to move, dark pelleted faeces.
	8	am	Quiet but alert, lying in hammock, pelleted faeces.
		pm	Quiet but active when stimulated.
	9	am	Quiet and huddled, alert when approached or stimulated, dark faeces.
		pm	Quiet and huddled on ladder, alert when stimulated, dark faeces.
	10	am	Quiet but alert, sitting on cage floor, active when stimulated, dark faeces.
		pm	Quiet but alert, sitting in hammock. Later, alert and active, aggressive, dark faeces.
	11	am	Alert, sitting on perch, dark loose faeces.
		pm	Quiet but alert when stimulated, dark faeces, vomit in cage.
	12	am	Quiet but alert, occasional activity, dark faeces.
		pm	Alert and fairly active, dark faeces.
	13	am	Alert and occasionally active, dark faeces.
		pm	Quiet and huddled in hammock, responds to external stimuli but reluctant to move.
	14	am	Alert and vocalising when approached, loose liquid faeces.
		pm	Quiet but alert, huddled at times, pale vomit in tray
	15	am	Quiet but alert, occasionally active, loose faeces.
		pm	Quiet but alert, occasionally active, vocalising, dark faeces, straining to urinate.
	16	am	Quiet but alert, occasionally active, dark faeces. Later; white vomit in tray.
		pm	Quiet, sitting in hammock, alert when stimulated, normal faeces.
	17	am	Quiet but alert, vocalising pale loose faeces.
		pm	Sacrificed for humane reasons.

APPENDIX 11

Individual clinical signs

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day, the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1) except where the animal did not survive beyond Day 0.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A5M	1	am	Alert, reluctant to move, lower part of wound weeping.
		pm	Quiet but alert .
	2	am	Subdued but alert.
		pm	Sacrificed for humane reasons.
A3M	1	am	Subdued but alert, sitting at back of cage, occasional activity, a short time later; animal lying on cage floor, appears uncomfortable.
		pm	Alert but not very active, moves when disturbed.
	2	am	Subdued but alert, sitting at back of cage, loose faeces, occasional activity.
		pm	Very quiet, subdued, huddled, reluctant to move even when stimulated, sacrificed for humane reasons.
A13M	1	am	Alert, occasional activity around cage.
		pm	Alert, not active, moves when disturbed.
	2	am	Alert, occasional activity, moves when disturbed, loose faeces.
		pm	Alert, moving around cage.
	3	am	Sitting on ladder, grooming self, normal faeces.
		pm	Alert, gentle activity, dark pelleted faeces.
	4	am	Quiet but alert, moving around cage, normal faeces.
		pm	Quiet but alert.
	5	am	Quiet but alert.
		pm	Alert, not very active.
	6	am	Quiet but alert, sitting on ladder.
		pm	Quiet and alert, sitting on ladder.
	7	am	Quiet but alert, some activity.
		pm	Quiet but alert.
	8	am	Quiet, sitting in corner of cage, alert when stimulated, occasional activity, pelleted faeces.
		pm	Alert and active, pelleted faeces.
	9	am	Quiet but alert, occasional activity, vocalisation, pelleted faeces.
		pm	Alert and active in cage, sometimes quiet.
	10	am	Quiet but alert, normal faeces.
		pm	Alert and active.
	11	am	Quiet but alert, active and threatening behaviour.
		pm	Alert and fairly active.
	12	am	Alert and active.
		pm	Quiet but alert, active in cage.
	13	am	Alert and reasonably active.
		pm	Alert, sitting in hammock.
	14	am	Bright and alert, scratching wound/surrounding area.
		pm	Alert and active, sitting on perch, grooming self.
	15	am	Bright, alert and active, lip-smacking.
		pm	Bright, alert and active, sitting on perch.
	16	am	Alert and fairly active.
		pm	Quiet but alert, active.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A13M (cont)	17	am	Alert and fairly active.
		pm	Alert and active.
	18	am	Alert and fairly active, pacing around cage floor.
		pm	Alert and active, pacing.
	19	am	Quiet but alert, sitting on perch, appears huddled.
		pm	Quiet but alert, sitting on ladder.
	20	am	Quiet but alert, sitting on ladder.
		pm	Quiet but fairly alert, moves when stimulated.
	21	am	Alert and active, sitting on perch.
		pm	Quiet but alert, occasional activity, dark pelleted faeces.
	22	am	Quiet but alert, sitting on perch, dark faeces.
		pm	No comment recorded.
	23	am	Quiet but alert, sitting on perch, grooming, normal faeces.
		pm	Alert and active.
	24	am	Alert, sitting on ladder.
		pm	Quiet but alert, sitting on perch.
	25	am	Alert and active when stimulated.
		pm	Bright, alert and active.
	26	am	Quiet but alert when stimulated.
		pm	Alert and active.
	27	am	Bright, alert and active.
		pm	Quiet but alert.
	28	am	Bright, alert and active.
		pm	Quiet but alert, sitting in hammock.
	29	am	Quiet but alert, sitting on ladder, active when stimulated.
		pm	Quiet but alert.
	30	am	Quiet but alert, moves when stimulated.
		pm	Quiet but alert, sitting on ladder, active when stimulated.
	31	am	Quiet but alert, sitting on perch, loose faeces.
		pm	Alert and active, loose faeces.
	32	am	Quiet but alert, sitting on perch, active when stimulated, soft/loose faeces.
		pm	Quiet but alert, normal faeces.
	33	am	Alert and active when stimulated, loose faeces.
		pm	Quiet but alert, sitting on ladder.
	34	am	Alert and active, quiet at times, pale loose faeces.
		pm	Alert and occasional activity, normal faeces.
	35	am	Alert and active, moving around cage.
		pm	Alert and fairly active.
	36	am	Alert and fairly active.
		pm	Quiet but alert, occasionally active.
	37	am	Quiet but alert.
		pm	Quiet but alert.
	38	am	Quiet but alert.
		pm	Quiet but alert, some activity.
	39	am	Quiet but alert.
		pm	Quiet but alert.
	40	am	Quiet but alert.
		pm	Quiet but alert, active when stimulated, abdomen swollen, loose faeces.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A13M (contd)	41	am	Quiet but alert, loose faeces.
		pm	Quiet but alert.
	42	am	Quiet but alert, normal faeces.
		pm	Quiet but alert, sitting on ladder, grooming.
	43	am	Quiet but alert when approached, huddled on perch.
		pm	Quiet but alert, sitting on ladder, some activity.
	44	am	Quiet but alert and active when stimulated, active.
		pm	Quiet but alert, active when stimulated, otherwise sitting on ladder, huddled, [subcutaneous oedema still prominent].
	45	am	Quiet and huddled, alert when stimulated, reluctant to move from ladder, slight swelling around both eyes, large subcutaneous swelling on abdomen.
		pm	Quiet and huddled, alert when stimulated.
	46	am	Quiet and huddled, reacts to external stimuli but reluctant to move, swelling around eyes, large abdominal swelling. Dark faeces.
		pm	Very subdued and huddled in cage, reluctant to move even when stimulated, sacrificed for humane reasons.
A9M	1	am	Quiet but alert, sitting on cage floor at front of cage, occasionally active
		pm	Lying on cage floor, grinding teeth.
			Overnight; huddled on cage floor, head resting on perch, reluctant to move even when stimulated, eyes rolling, heavy lidded.
	2	am	Sitting on cage floor leaning against side, eyes rolling, heavy lidded, reluctant to move even when stimulated. Sacrificed for humane reasons.
A1M	1	am	Lying on cage floor, becomes alert and sits up when stimulated.
		pm	Quiet but alert, sitting on cage floor, dark faeces.
	2	am	Alert and fairly active, dark faeces.
		pm	Alert but not very active, sitting in corner of cage, normal faeces.
	3	am	Alert and occasionally active.
		pm	Quiet but alert.
	4	am	Alert, sitting on ladder, grooming.
		pm	Alert, lying on ladder, active when stimulated.
	5	am	Alert and fairly active.
		pm	Alert and occasionally active.
	6	am	Alert and fairly active, loose faeces.
		pm	Alert but not very active, normal faeces.
	7	am	Alert and active.
		pm	Quiet but alert, some activity.
	8	am	Bright, alert and active, fluid build up in scrotum and lower abdomen.
		pm	Quiet but alert, little activity.
	9	am	Quiet but alert, lying on ladder, aggressive.
		pm	Alert, not very active.
	10	am	Alert and active, sitting on ladder.
		pm	Quiet but alert, sitting on ladder, some activity.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A1M (contd)	11	am	Alert and active, sitting on cage floor.
		pm	Quiet but alert, sitting on perch.
	12	am	Quiet but alert when stimulated.
		pm	Quiet but alert, fluid build up around scrotum and wound.
	13	am	Bright and alert, occasionally active, fluid build up in scrotum, lower abdomen and tops of legs.
		pm	Alert and fairly active.
	14	am	Bright, alert and active, dark pelleted faeces, fluid build up in scrotum, lower abdomen and tops of legs.
		pm	Cuddling pairing partner.
	15	am	Quiet but alert, active when stimulated.
		pm	Alert.
	16	am	Quiet but alert, active when stimulated.
		pm	Quiet but alert, straining, does not appear to be urinating easily.
	17	am	Alert and active.
		pm	Quiet but alert, active, moving around cage.
	18	am	Quiet but alert, sitting on perch, observed vomiting, , slightly active, dark faeces.
		pm	Quiet but alert, sitting on perch, normal faeces.
	19	am	Alert and active, sitting on ladder.
		pm	Alert, grooming.
	20	am	Alert and active, moving around cage.
		pm	Bright, alert and active, grooming.
	21	am	Quiet but alert, dried blood around scrotum.
		pm	Alert, fairly active.
	22	am	Alert and active, moving around cage.
		pm	Alert, occasionally active.
	23	am	Quiet but alert, crouched in corner.
		pm	Quiet but alert.
	24	am	Alert, some activity.
		pm	Alert, fairly active, sitting on perch.
	25	am	Alert and active, loose faeces.
		pm	Alert and fairly active, normal faeces, occasionally unsteady.
	26	am	Alert and active.
		pm	Alert and active.
	27	am	Alert and active.
		pm	Quiet but alert.
	28	am	Quiet but alert.
		pm	Quiet but alert, sitting on ladder.
	29	am	Bright, alert and active.
		pm	Quiet, sitting on ladder, alert and active when stimulated.
	30	am	Quiet but alert, aggressive posture when stimulated/approached.
		pm	Quiet but alert, sitting on ladder, grooming.
	31	am	Quiet but alert, aggressive when approached, pelleted faeces.
		pm	Quiet but alert, sitting at front of cage, threatening behaviour.
	32	am	Quiet but alert, slightly active, grooming, sitting on ladder, reacts to external stimuli, dark faeces.
		pm	Quiet but alert, active, normal faeces.
	33	am	Alert and slightly active, sitting on ladder, grooming, dark faeces.
		pm	Alert, occasionally active, sitting on perch, appears calm.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A1M (contd)	34	am	Alert, moving around cage when stimulated, very loose faeces.
		pm	Alert, occasional activity, loose faeces.
	35	am	Alert and active when stimulated, grooming, loose faeces.
		pm	Alert and active, pacing around cage, grooming, normal faeces. Later, Quiet but alert, grooming self.
	36	am	Bright and alert, occasionally active, sitting on ladder.
		pm	Alert and active when stimulated, sitting on ladder, grooming.
	37	am	Alert, aggressive, sitting on ladder, grooming, loose faeces.
		pm	Quiet but alert, sitting on cage floor, soft faeces.
	38	am	Quiet but alert, aggressive when approached, build up of fluid around abdomen, loose faeces.
		pm	Quiet but alert, occasionally active, loose faeces.
	39	am	Alert, loose faeces.
		pm	Alert, threatening when stimulated, sitting on perch.
	40	am	Quiet but alert, active when stimulated, abdomen appears less distended but still some fluid build up around wound, normal faeces.
		pm	Quiet but alert, occasionally active.
	41	am	Alert and fairly active, soft/loose faeces, fluid build up still visible around wound, abdomen appears less distended.
		pm	Alert, loose faeces.
	42	am	Quiet but alert, active when stimulated, sitting in corner of cage, laboured respiration. Later; very laboured respiration especially when handled, vocalisation, subdued and huddled, reluctant to move, unusual postures, unsteady, very slow movements when returned to cage. Sacrificed for humane reasons.
A17M	1	am	Bright and alert, sitting/lying on ladder.
		pm	Quiet but alert, sitting on perch.
	2	am	Alert when stimulated, sitting on ladder.
		pm	Alert when stimulated.
	3	am	Alert when stimulated, sitting on ladder, pelleted faeces.
		pm	Quiet and huddled against ladder, alert when stimulated.
	4	am	Alert, not very active unless stimulated, sitting on ladder, soft faeces.
		pm	Alert, active when stimulated, sitting on ladder, loose faeces.
	5	am	Quiet but alert, responding to external stimuli, loose faeces.
		pm	Quiet but alert, responding to external stimuli, soft faeces.
	6	am	Quiet but alert, responding to external stimuli, soft faeces.
		pm	Alert and active, responding to external stimuli.
	7	am	Quiet but alert, normal faeces.
		pm	Quiet but alert, soft faeces.
	8	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert, little activity.
	9	am	Quiet but alert, active when stimulated, sitting on ladder, normal faeces.
		pm	Alert, sitting on ladder.
	10	am	Alert, sitting on ladder.
		pm	Quiet but alert, active when stimulated, lying on ladder.
	11	am	Alert, sitting on ladder.
		pm	Quiet and huddled, reluctant to move.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A17M (contd)	12	am	Alert and active.
		pm	Quiet but alert, lying on ladder, aggressive when approached.
	13	am	Quiet but alert if stimulated, occasionally active, small fluid build up at bottom of wound.
		pm	Alert and fairly active.
	14	am	Quiet but alert, occasionally active.
		pm	Grooming, occasionally playful.
	15	am	Quiet, lying down on ladder, alert but not active when stimulated.
		pm	Alert and active.
	16	am	Alert and active, moving around cage.
		pm	Alert and active, sitting on ladder.
	17	am	Alert and active when stimulated.
		pm	Alert, moving around cage.
	18	am	Alert and active, mildly aggressive, dark faeces.
		pm	Alert and active, sitting on ladder, occasionally aggressive when stimulated.
	19	am	Alert when stimulated, sitting on ladder, quiet, normal faeces, [a little quiet].
		pm	Alert, sitting on ladder, grooming.
	20	am	Alert but generally quiet, sitting on ladder.
		pm	Alert and fairly active.
	21	am	Quiet but alert, sitting on ladder.
		pm	Alert and fairly active.
	22	am	Quiet but alert, sitting on ladder.
		pm	Alert and fairly active.
	23	am	Alert and active.
		pm	Alert and fairly active.
	24	am	Quiet, lying down on cage floor, alert when stimulated. Later; subdued, lying on cage floor, very unsteady/uncoordinated when stimulated, pale gums. Sacrificed for humane reasons.
A18M	1	am	Quiet, lying on cage floor, moves when stimulated.
		pm	Quiet and huddled against ladder, alert when stimulated.
	2	am	Very quiet and huddled, reluctant to move even when stimulated, appears bright eyed and looking around, lying across ladder.
		pm	Subdued and huddled, little reaction to stimuli, sacrificed for humane reasons.
A16F	1	am	Bright and alert to external stimuli.
		pm	Quiet but alert. Small subcutaneous swelling and bruising at injection site on right side of back.
	2	am	Quiet but alert, active when stimulated, sitting on ladder, grooming. Large bruise on left lower leg.
		pm	Quiet but alert, sitting on ladder.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A16F (contd)	3	am	Quiet but alert, quite active, normal faeces.
		pm	Quiet but alert, moving around cage.
	4	am	Quiet but alert, active when stimulated.
		pm	Quiet but alert when stimulated, slightly subdued, pelleted faeces.
	5	am	Quiet but alert when stimulated, normal faeces.
		pm	Very alert, gentle activity, fluid build up around wound.
	6	am	Quiet but alert, sitting across ladder, occasionally active.
		pm	Quiet but alert, becoming active, dark pelleted faeces.
	7	am	Quiet but alert, occasionally active, normal faeces.
		pm	Very observant, sitting on hammock, relaxed and alert, occasionally playful.
	8	am	Quiet but alert, becomes active when stimulated.
		pm	Alert and active, normal faeces.
	9	am	Quiet but alert, quite active, sitting in hammock, very relaxed.
		pm	Quiet but alert, quieter than normal, sitting on ladder, unusual sprawled posture.
	10	am	Alert, sitting in hammock.
		pm	Quiet but alert, slightly active, sitting on perch, dark faeces.
	11	am	Quiet but alert, reacts to external stimuli, sitting in hammock, dark faeces.
		pm	Quiet but alert, sitting on perch, normal faeces.
	12	am	Alert and active, moving around cage.
		pm	Quiet but alert, sitting on perch, grooming partner.
	13	am	Alert and active, moving around cage.
		pm	Bright, alert and active, fluid build up in lower abdomen.
	14	am	Quiet but alert, active when disturbed.
		pm	Quiet but alert, occasional activity.
	15	am	Quiet but alert, sitting in hammock.
		pm	Alert and fairly active.
	16	am	Quiet but alert, sitting in hammock.
		pm	Alert, some activity.
	17	am	Alert and fairly active.
		pm	Alert and active, moving around cage.
	18	am	Alert and active.
		pm	Alert and active.
	19	am	Alert and active.
		pm	Quiet but alert, active when stimulated.
	20	am	Alert and active when stimulated.
		pm	Quiet but alert when stimulated.
	21	am	Quiet but alert.
		pm	Quiet but alert, active when stimulated, sitting on ladder. Later; slight upper body tremors, alert, trying to sleep.
	22	am	Quiet but alert, occasionally active when stimulated.
		pm	Quiet but alert, sitting on perch, occasionally straining and sometimes active.
	23	am	Quiet but alert, sitting on ladder, occasionally active, sneezing whilst cage being cleaned.
		pm	Alert and active.
	24	am	Quiet but alert, sitting on ladder, moves when stimulated.
		pm	Quiet but alert, sitting on ladder, straining, responsive to stimuli.
	25	am	Quiet but alert, sitting on hammock, reacts to external stimuli.
		pm	Quiet but alert, fairly active, loose faeces.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A16F (contd)	26	am	Quiet and huddled on ladder, aggressive when approached, grooming self, normal faeces.
		pm	Quiet and huddled on hammock, occasionally active.
	27	am	Quiet but alert, occasionally active.
		pm	Quiet but alert, occasionally active.
	28	am	Quiet but alert, sitting on hammock.
		pm	Quiet but alert, sitting on perch, active when stimulated.
	29	am	Quiet and huddled in hammock, reluctant to react to external stimuli
		pm	Quiet but alert, sitting in hammock.
	30	am	Quiet but alert, active when stimulated, sitting on ladder.
		pm	Quiet but alert, sitting on perch, active when stimulated.
	31	am	Quiet but alert, moves when approached, abdomen distended.
		pm	Alert, some activity.
	32	am	Alert and fairly active.
		pm	Vomit in tray, quiet but alert, sitting in hammock.
	33	am	Quiet but alert, sitting on cage floor, moves onto perch when stimulated, abdomen distended, fluid build up around wound, soft faeces at dose.
		pm	Quiet, lying on ladder, moves when stimulated, loose faeces.
	34	am	Quiet and huddled, alert when stimulated, dark loose faeces, subcutaneous fluid build up around wound.
		pm	Quiet, lying across ladder, dark loose/liquid faeces. Sacrificed for humane reasons.
A12F	1	am	Quiet but alert, sitting on cage floor, heavy lidded.
		pm	Quiet but alert.
	2	am	Quiet but alert, sitting on ladder, large bruise and swelling on left thigh.
		pm	Alert.
	3	am	Alert, sitting on ladder.
		pm	Alert, moving around cage.
	4	am	Alert, sitting on ladder, moves when stimulated.
		pm	Quiet but alert, sitting on ladder, dark faeces.
	5	am	Quiet but alert, normal faeces.
		pm	Quiet but alert, lying on ladder, moves when stimulated, pelleted faeces.
	6	am	Bright, alert and active, normal faeces.
		pm	Alert and fairly active.
	7	am	Alert, slightly active, sitting on perch, dark faeces.
		pm	Alert, sitting in hammock, grooming.
	8	am	Alert but generally quiet, becomes active when stimulated, pelleted faeces.
		pm	Alert and active, normal faeces.
	9	am	Alert and active when stimulated.
		pm	Alert and active.
	10	am	Alert and active, moving around cage.
		pm	Alert and active, grooming, dark faeces.
	11	am	Quiet but alert, sitting on perch, normal faeces.
		pm	Alert and active.
	12	am	Alert and active, interested in surroundings.
		pm	Alert and active, grooming pairing partner, licking cage.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A12F (contd)	13	am	Alert and active, moving around cage.
		pm	Bright, alert and active.
	14	am	Alert and active, aggressive when disturbed.
		pm	Alert and active.
	15	am	Alert and active moving around cage.
		pm	Alert and active, moving around cage.
	16	am	Alert and active.
		pm	Alert and fairly active.
	17	am	Alert and active.
		pm	Alert and active, sitting on perch, occasionally quiet.
	18	am	Alert and active.
		pm	Alert and active.
	19	am	Alert and active.
		pm	Alert and active, moving around cage.
	20	am	Alert and active.
		pm	Alert and active.
	21	am	Alert and active.
		pm	Quiet but alert, huddled with pairing partner. Later; body tremors noted during dosing, alert and lying on ladder nestling.
	22	am	Bright, alert and active.
		pm	Bright, alert and active.
	23	am	Alert and active.
		pm	Alert and active interacting with pairing partner.
	24	am	Alert and active.
		pm	Alert and active, hanging from roof of cage.
	25	am	Alert and active, sitting on perch.
		pm	Alert and active.
	26	am	Alert and active, moving around cage floor.
		pm	Alert and active, moving around cage. Later, tremors.
	27	am	Alert and active.
		pm	Alert and active.
	28	am	Quiet but alert, active, sometimes moving around cage.
		pm	Quiet but alert.
	29	am	Quiet but alert, lying across ladder, grinding teeth.
		pm	Alert, grooming, moving around cage, grooming pairing partner.
	30	am	Alert and active, pacing around cage.
		pm	Alert and active.
	31	am	Alert and active.
		pm	Alert and active, moving around cage.
	32	am	Alert and active, moving around cage.
		pm	Alert and active, threatening when approached, playful with partner.
	33	am	Alert and active.
		pm	Alert and active, moving around cage.
	34	am	Bright, alert and active.
		pm	Alert and active.
	35	am	Bright, alert and active.
		pm	Bright, alert and active.
	36	am	Bright, alert and active.
		pm	Alert and active.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A12F (contd)	37	am	Bright, alert and active.
		pm	Bright and alert, grooming.
	38	am	Bright, alert and active.
		pm	Quiet, huddled with pairing partner, eyes closed.
	39	am	Bright, alert and active.
		pm	Alert and active.
	40	am	Alert and active, moving around cage.
		pm	Quiet but alert, occasionally active, loose/liquid faeces.
	41	am	Alert and active, moving around cage, very loose faeces.
		pm	Quiet but alert, huddled on ladder, grinding teeth, liquid faeces.
	42	am	Alert and active, moving around cage when stimulated, loose faeces.
		pm	Quiet but alert, active when stimulated, liquid faeces.
	43	am	Subdued but alert, lying on ladder, slow movements when stimulated, grinding teeth, loose faeces.
		pm	Alert, quite active, grooming and washing hands, very loose faeces.
	44	am	Alert and fairly active, liquid faeces.
		pm	Quiet but alert, loose/liquid faeces.
	45	am	Quiet but alert, some periods of activity, very loose faeces.
		pm	Quiet but alert when stimulated, sitting on ladder, normal faeces.
	46	am	Quiet but alert, active when stimulated, very loose faeces, abdomen appears swollen.
		pm	Alert, not very active, sitting on ladder.
	47	am	Quiet but alert, sitting/lying on ladder, normal faeces.
		pm	Alert, vocalising.
	48	am	Quiet but alert, biting top of ladder.
		pm	Quiet but alert, sitting on ladder, reacts to external stimuli, active, dark faeces.
	49	am	Quiet but alert, active when stimulated, normal faeces.
		pm	Quiet and huddled, alert to external stimuli.
	50	am	Quiet and huddled, sitting on perch, vomit in cage and tray.
		pm	Quiet but alert, active when stimulated, unusual posture.
	51	am	Subdued and huddled, lying on ladder, reluctant to move even when stimulated.
		pm	Subdued and huddled, reluctant to move, large oedema on abdomen and around tail. Following pairing with partner, animal is more alert and moving slowly around cage, grooming. Later; sacrificed for humane reasons.
A8F	1	am	Quiet but alert, appears tired, aggressive when stimulated.
		pm	Not alert due to pethidine dose. Sacrificed for humane reasons.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A96M	1	am	Quiet but alert, moving around when stimulated.
		pm	Quiet and huddled, leaning against side of cage, heavy lidded, appears tired/drowsy.
	2	am	Quiet and alert, walking around cage, fairly active.
		pm	Quiet but alert, lying on ladder.
	3	am	Quiet but alert, huddled in corner of cage, active when stimulated.
		pm	Active and aggressive.
	4	am	Quiet but alert, occasional activity.
		pm	Quiet but alert to external stimuli, grooming.
	5	am	Quiet but alert, scratching and grooming on ladder. Later; lying on ladder, aggressive when approached.
		pm	Quiet and huddled with pairing partner, appears asleep.
	6	am	Alert and active, moving around cage.
		pm	Alert, grooming partner.
	7	am	Alert, sitting at front of cage, interested in surroundings.
		pm	Alert, slightly active, sitting on ladder, grooming self, dark faeces.
	8	am	Quiet but alert, sitting on ladder, active when stimulated, picking at scar, normal faeces.
		pm	Quiet but alert, cuddling with partner.
	9	am	Quiet but alert when stimulated, lying on ladder.
		pm	Quiet but alert, grooming partner.
	10	am	Quiet, reluctant to move, sitting on perch, aggressive when stimulated.
		pm	Quiet but alert, lying on ladder.
	11	am	Quiet, sitting on ladder.
		pm	Quiet, sitting on ladder.
	12	am	Quiet but occasionally active.
		pm	Active when stimulated, lying on ladder, aggressive when approached.
	13	am	Quiet but alert, sitting in hammock, loose faeces.
		pm	Quiet but alert, sitting in hammock facing back of cage, loose faeces.
	14	am	Quiet but alert, aggressive when approached, slightly active, sitting in hammock.
		pm	Quiet but alert, active, moving around cage.
	15	am	Resting, lying on ladder, aggressive when approached, vomit in cage.
		pm	Quiet and huddled, head between knees.
	16	am	Alert, sitting on perch, normal faeces.
		pm	Quiet but alert, huddled with pairing partner, active when stimulated, liquid faeces.
	17	am	Quiet but alert, aggressive, active when stimulated, loose faeces, vomit on perch.
		pm	Quiet but alert, sitting on ladder, active when stimulated, liquid faeces.
	18	am	Quiet but alert, active when stimulated, liquid faeces.
		pm	Alert, gentle activity, loose faeces.
	19	am	Alert, occasional activity, liquid faeces, bruise on right thigh.
		pm	Subdued and huddled, reluctant to move, swelling around both eyes, swollen abdomen, liquid faeces. Sacrificed for humane reasons .
A95M	1	am	Quiet but alert, sitting on tray.
		pm	Quiet and lying down, alert to external stimuli.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day No.		Observation
A95M (contd)	2	am	Quiet but alert, sitting on box, slightly active.
		pm	Quiet but alert, sitting on ladder, bruise on right forearm, pelleted faeces.
	3	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert, sitting on perch, active when stimulated.
	4	am	Quiet but alert, sitting upright on perch.
		pm	Quiet but alert to external stimuli, grooming partner.
	5	am	Quiet but alert, grooming self on ladder, slightly active, mucus faeces.
		pm	Quiet but alert, huddled with partner, appears asleep, normal faeces.
	6	am	Alert and active when stimulated. Later; animal retching and vomiting.
		pm	Cuddling with pairing partner.
	7	am	Quiet but alert, sitting on cage floor, huddled, active when stimulated.
		pm	Quiet but alert, slightly active, dark faeces.
	8	am	Quiet but alert, sitting on cage floor, huddled, normal faeces.
		pm	Cuddling with pairing partner.
	9	am	Subdued and huddled on cage floor, reluctant to move even when stimulated, piloerection, soft faeces.
		pm	Quiet but alert, sitting on perch, grooming, normal faeces.
	10	am	Alert and moving around cage, loose faeces.
		pm	Quiet but alert, huddled on ladder, active when stimulated.
	11	am	Alert and active, normal faeces.
		pm	Quiet but alert.
	12	am	Quiet but alert, sitting on ladder, active when stimulated.
		pm	Quiet but alert, sitting on ladder, appears huddled, active when stimulated.
	13	am	Quiet but alert, sitting on ladder, lip smacking.
		pm	Quiet but alert, sitting on ladder, reacts to external stimuli.
	14	am	Quiet but alert, slightly aggressive when approached, dark faeces.
		pm	Quiet and huddled, sitting on perch, responds to external stimuli.
	15	am	Quiet but alert, mildly aggressive when approached, sitting on cage floor leaning against cage door.
		pm	Quiet and huddled.
	16	am	Quiet but alert, huddled, vocalising, normal faeces.
		pm	Quiet and huddled with pairing partner, sitting on ladder, active when stimulated. Liquid faeces.
	17	am	Quiet, not very alert, huddled on perch. Aggressive when stimulated, liquid faeces.
		pm	Quiet and huddled, sitting on ladder, active when stimulated.
	18	am	Subdued and huddled, becomes alert when stimulated, abdomen and scrotum appear swollen, loose faeces.
		pm	Alert, sitting on perch, cuddling pairing partner.
	19	am	Quiet but alert, occasionally active, normal faeces. Later, subdued and huddled, unsteady when moving, scrotum swollen. Sacrificed for humane reasons.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day No.		Observation
A2F	0	pm	Following surgery; animal subdued, sitting on box floor supporting itself on cage front, reacts to external stimuli. Later; resting, leaning against bars, huddled, occasional slow movements. Subdued and unresponsive, no reaction to external stimuli, shallow respiration, cold to touch. Animal in collapsed state. Sacrificed for humane reasons.

APPENDIX 11

Individual clinical signs

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day, the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1) except where the animal did not survive beyond Day 0.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y255M	1	am	Quiet but alert.
		pm	Quiet but alert.
	2	am	Quiet but alert, red discoloured urine.
		pm	Quiet but alert, reluctant to move, huddled over perch, alert when stimulated.
	3	am	Bright and alert, sitting on perch at front of cage.
		pm	Quiet but alert, sitting on cage floor.
	4	am	Alert and fairly active, occasionally huddled, dark faeces.
		pm	Quiet and huddled on cage floor, reluctant to move, alert when stimulated
	5	am	Alert, sitting on perch, black faeces.
		pm	Quiet, sitting on cage floor, alert when stimulated
	6	am	Quiet but alert, occasionally active, dark faeces.
		pm	quiet but alert, occasionally active, sitting in hammock
	7	am	Quiet but alert, reluctant to move, normal faeces.
		pm	Quiet but alert, occasionally active.
	8	am	Quiet but alert, moves when approached, pale loose/liquid faeces.
		pm	Quiet but alert, moves when stimulated.
	9	am	Quiet but alert, normal faeces.
		pm	Quiet but alert, sitting on cage floor.
	10	am	Quiet but alert, occasionally active, dark faeces.
		pm	Alert, fairly active, dark faeces.
	11	am	Quiet but alert, occasionally active, pale loose faeces.
		pm	Alert, active when approached.
	12	am	Quiet but alert, sitting on ladder, active when stimulated, normal faeces.
		pm	Alert and active.
	13	am	Alert and active.
		pm	Alert and gentle activity.
	14	am	Alert and active.
		pm	Alert and active.
	15	am	Alert and active.
		pm	Alert and active.
	16	am	Alert and fairly active.
		pm	Alert and active.
	17	am	Alert and active.
		pm	Alert and active when approached.
	18	am	Alert and active.
		pm	Alert and active when stimulated.
	19	am	Alert and active.
		pm	Alert and active.
	20	am	Alert and fairly active.
		pm	Alert and active.
	21	am	Alert and fairly active.
		pm	Alert and fairly active.
	22	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert, occasionally active.
	23	am	Quiet but alert.
		pm	Alert, occasionally active.
	24	am	Quiet but alert, occasionally active.
		pm	Quiet but alert, sitting on cage floor.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y255M (cont)	25	am	Quiet but alert, occasionally active.
		pm	Alert, gentle activity.
	26	am	Alert and occasionally active, dark faeces.
		pm	Quiet and huddled on perch, alert when approached but reluctant to move, red stained urine.
	27	am	Quiet and huddled on ladder, reasonably alert, moves when approached.
		pm	Quiet and huddled in corner of cage, reluctant to move, later; alert, gentle activity.
	28	am	Alert, some movement, dark faeces.
		pm	Quiet but alert, sitting on perch, active when stimulated, loose faeces.
	29	am	Quiet but alert, movement when stimulated, loose faeces.
		pm	Quiet and huddled on ladder, reacts to external stimuli.
	30	am	Quiet but alert.
		pm	Quiet and huddled over ladder, alert when stimulated, pale liquid faeces., swelling around both eyes.
	31	am	Quiet and alert, slightly active, difficulty passing urine, yellow liquid faeces.
		pm	Alert and active, vomit in tray.
	32	am	Quiet but alert, vomit in tray.
		pm	Quiet and huddled on perch, alert when stimulated, liquid faeces.
	33	am	Quiet and subdued, little reaction when stimulated, liquid faeces.
		pm	Sacrificed for humane reasons.
Y243M	1	am	Quiet but alert, sitting upright.
		pm	Quiet, sitting on perch, leaning against cage front, eyes partially closed, alert when stimulated, reluctant to move.
	2	am	Quiet and huddled, slow movements, vocalisation, dark pelleted faeces.
		pm	Abdomen distended. Sacrificed for humane reasons.
Y242F	1	am	Quiet but alert and active, sitting on perch, threatening behaviour.
		pm	Quiet but alert, sitting on ladder, occasionally active, grinding teeth.
	2	am	Quiet but alert.
		pm	Quiet but alert, dark faeces.
	3	am	Quiet but alert, dark faeces.
		pm	Quiet but alert, dark faeces.
	4	am	Quiet but alert, sitting in hammock, dark faeces.
		pm	Alert, gentle activity.
	5	am	Quiet but alert, sitting in hammock, dark faeces.
		pm	Quiet but alert, dark faeces., more active than morning.
	6	am	Quiet but alert, sitting in hammock, reluctant to move, dark faeces.
		pm	Sitting in hammock, reluctant to move, normal faeces., later; alert, active if approached.
	7	am	Quiet but alert, sitting in hammock, active when approached, dark faeces.
		pm	Quiet but alert, sitting on ladder, threatening behaviour, normal faeces.
	8	am	Quiet but alert.
		pm	Quiet but alert, occasionally active.
	9	am	Quiet but alert, occasionally active.
		pm	Quiet but alert, dark faeces.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y242F (cont)	10	am	Quiet but alert, reacts to external stimuli, normal faeces.
		pm	Alert and active, good response to stimuli, grooming self.
	11	am	Quiet but alert, occasionally active, dark faeces.
		pm	Quiet but alert, dark faeces.
	12	am	Quiet but alert, moderately active, dark faeces.
		pm	Quiet but alert, dark faeces.
	13	am	Alert and active, dark pelleted faeces.
		pm	Quiet but alert and active, dark faeces.
	14	am	Sitting in hammock, reluctant to move when stimulated, normal faeces.
		pm	Alert and active when stimulated.
	15	am	Sitting on ladder, awake and fairly alert, frequently moving around cage.
		Pm	Alert and active, grooming partner.
	16	am	Quiet but alert, slightly active, dark faeces.
		pm	Alert.
	17	am	Moving around cage, normal faeces.
		pm	Alert, sitting on ladder.
	18	am	Quiet but alert, sitting in hammock.
		pm	Quiet but alert.
	19	am	Quiet but alert, slightly active, sitting in hammock, dark faeces.
		pm	Quiet but alert, sitting on ladder in unusual posture, normal faeces.
	20	am	Quiet but alert, sitting in hammock.
		pm	Quiet but alert. Slightly active, dark faeces.
	21	am	Alert and active when stimulated, normal faeces.
		pm	Alert and active, dark faeces.
	22	am	Alert, sitting on perch, grooming self, normal faeces.
		pm	Alert and active.
	23	am	Alert, sitting at front of cage.
		pm	Alert and active.
	24	am	Alert, sometimes active, sitting on perch.
		pm	Quiet and huddled on ladder, dark pelleted faeces.
	25	am	Alert and active, walking around cage, normal faeces.
		pm	Alert , occasional activity, dark pelleted faeces.
	26	am	Quiet but alert, occasional activity, dark pelleted faeces.
		pm	Alert, slight active, dark pelleted faeces.
	27	am	Alert and active when stimulated, dark pelleted faeces.
		pm	Quiet but alert, sitting on ladder, normal faeces.
	28	am	Alert, occasional activity, dark faeces.
		pm	Alert and fairly active, dark faeces.
	29	am	Quiet but alert, normal faeces.
		pm	Quiet but alert, moving around cage.
	30	am	Alert and fairly active, dark pelleted faeces.
		pm	Alert and occasionally active, normal faeces.
	31	am	Alert, gentle activity.
		Pm	Alert and active, sitting on perch, dark faeces.
	32	am	Alert and active, normal faeces.
		pm	Alert and active.
	33	am	Alert and occasionally active, dark faeces.
		pm	Alert and gentle activity.
	34	am	Quiet but alert, grooming self, occasionally active, pelleted faeces.
		pm	Alert and reasonably active, normal faeces.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y242F (cont)	35	am	Alert and active.
		pm	Alert but not active, sitting on ladder.
	36	am	Alert and active.
		pm	Quiet but alert and occasionally active, sitting on ladder.
	37	am	Alert and active.
		pm	Alert and fairly active, pelleted faeces.
	38	am	Alert and active, normal faeces.
		pm	Alert, not very active.
	39	am	Quiet but alert, sitting huddled on ladder.
		pm	Quiet but alert.
	40	am	Quiet but alert, moving around cage.
		pm	Alert and active.
	41	am	Alert and active.
		pm	Quiet but alert, not active.
	42	am	Quiet but alert, sitting on ladder.
		pm	Quiet but alert, moving around cage.
	43	am	Quiet but alert, occasional activity.
		pm	Quiet but alert.
	44	am	Quiet but alert, occasional activity.
		pm	Quiet but alert, sitting on ladder, little activity.
	45	am	Quiet but alert, sitting on ladder.
		pm	Alert and active, climbing on ladder.
	46	am	Alert, occasional activity.
		pm	Alert and active.
	47	am	Quiet but alert and active, pelleted faeces.
		pm	Alert and active, normal faeces.
	48	am	Alert and fairly active.
		pm	Alert and fairly active
	49	am	Alert and reasonably active, pelleted faeces.
		pm	Alert and fairly active, normal faeces.
	50	am	Bright and alert, sitting in hammock, pelleted faeces.
		pm	Alert and active, sitting on perch, normal faeces.
	51	am	Bright, alert and active, pelleted faeces.
		pm	Bright, alert and active, sitting on perch, hugging pairing partner, normal faeces.
	52	am	Quiet but alert, sitting on ladder.
		pm	Quiet and active, pelleted faeces.
	53	am	Quiet but alert, sitting on ladder, normal faeces.
		pm	Quiet but alert and active, aggressive.
	54	am	Alert, active when stimulated, sitting on ladder, grooming, soft faeces, vomit in tray.
		pm	Alert, sitting on perch, active when stimulated, grooming pairing partner
	55	am	Quiet but alert, sitting on ladder, threatening behaviour, pelleted faeces.
		pm	Active and alert.
	56	am	Alert, sitting on ladder, not very active, normal faeces.
		pm	Alert and active when stimulated.
	57	am	Quiet but alert, sitting on ladder.
		pm	Alert and active.
	58	am	Alert and fairly active.
		pm	Alert and active.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y242F (cont)	59	am	Alert and not very active.
		pm	Alert, [hunched posture and teeth grinding].
	60	am	Alert, sitting on ladder, not very active.
		pm	Alert, sitting on ladder, not very active.
	61	am	Quiet but alert, sitting on ladder.
		pm	Quiet and huddled on ladder, alert if stimulated.
	62	am	Alert and active.
		pm	Very alert, active if stimulated.
	63	am	Bright, alert and active, sitting on ladder.
		pm	Alert, occasional activity, dark faeces.
	64	am	Quiet but mostly alert and active, normal faeces.
		pm	Alert and active.
	65	am	Quiet but alert.
		pm	Alert, not very active.
	66	am	Quiet but alert.
		pm	Bright and active.
	67	am	Quiet but alert.
		pm	Alert and slightly active, sitting on perch, dark faeces.
	68	am	Quiet but alert, sitting on ladder, moves when stimulated, swelling above both eyes, normal faeces.
		pm	Alert and active.
	69	am	Quiet but alert, sitting on ladder, active, dark faeces.
		pm	Alert and active, aggressive.
	70	am	Quiet but alert, active when stimulated, green/yellow vomit.
		pm	Subdued, huddled, slow movements when stimulated, unsteady and uncoordinated, pale loose faeces.
	71	am	Lying on cage floor, little response to stimuli, dilated pupils, cold to touch, rapid respiration in lower abdomen, occasional vocalisation, vacant expression, motionless. Sacrificed for humane reasons.
Y252F	1	am	Quiet but alert.
		pm	Quiet but alert.
	2	am	Quiet but alert.
		pm	Quiet but alert, dark faeces.
	3	am	Alert and active, occasionally quiet, sitting in unusual stretched posture, dark faeces.
		pm	Alert, gentle activity.
	4	am	Alert and reasonably active, dark faeces.
		pm	Alert and reasonably active, dark faeces.
	5	am	Quiet but alert, occasionally active, grooming self, dark pelleted faeces.
		pm	Asleep on perch/ladder, normal faeces. Later; alert, gently activity.
	6	am	Quiet but alert, slightly active, sitting on ladder, dark faeces.
		pm	Alert and fairly active, dark faeces.
	7	am	Alert and active, normal faeces.
		pm	Quiet but alert, sitting on ladder, dark pelleted faeces.
	8	am	Quiet but alert, sitting in hammock, dark pelleted faeces.
		pm	Quiet but alert, dark pelleted faeces.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y252F (cont)	9	am	Quiet and moderately alert, sitting in hammock, dark faeces.
		pm	Quiet but alert, hanging on cage top, sometimes active, normal faeces.
	10	am	Quiet but alert, sitting in hammock, dark faeces.
		pm	Quiet but alert, sitting in hammock, dark faeces.
	11	am	Quiet but alert, moderately active, sitting on ladder, dark faeces.
		pm	Quiet but alert, occasionally active, dark faeces.
	12	am	Quiet and huddled against ladder, reluctant to move even when approached, dark faeces.
		pm	Quiet but alert, sitting in hammock, dark pelleted faeces.
	13	am	Sitting in hammock, reluctant to move when stimulated, normal faeces.
		pm	Alert and active.
	14	am	Quiet but alert, sitting in hammock, dark faeces.
		pm	Alert and active, loose faeces.
	15	am	Quiet but alert, loose faeces.
		pm	Quiet but alert when stimulated, loose faeces.
	16	am	Quiet but alert, loose faeces.
		pm	Quiet but alert, normal faeces.
	17	am	Quiet but alert, dark faeces.
		pm	Quiet but alert, sitting in hammock, dark faeces.
	18	am	Quiet and drowsy, reacts to external stimuli but is reluctant to move, dark faeces.
		pm	Quiet but alert and active.
	19	am	Quiet but alert, very relaxed, lying in hammock grooming self, loose faeces.
		pm	Quiet but alert, grooming in hammock, loose faeces.
	20	am	Sitting in hammock, relaxed, loose faeces.
		pm	Alert and active, grooming, normal faeces.
	21	am	Alert, sitting on ladder.
		pm	Quiet but alert, loose faeces.
	22	am	Sitting on perch, grooming self, loose faeces., [abnormal posture].
		pm	Quiet but alert and active when stimulated.
	23	am	Quiet but alert, grooming self in hammock, soft faeces.
		pm	Quiet and huddled in hammock, reluctant to move, dark faeces.
	24	am	Alert and quite active, dark faeces.
		pm	Alert and sometimes active, dark faeces.
	25	am	Quiet but alert, occasionally active, dark loose faeces.
		pm	Quiet but alert when stimulated.
	26	am	Quiet but alert when stimulated, liquid faeces.
		pm	Quiet but alert, reluctant to move.
	27	am	Quiet and huddled, sitting in hammock, alert when stimulated, normal faeces.
		pm	Quiet but alert, dark faeces.
	28	am	Quiet but alert, sitting on ladder, normal faeces.
		pm	Alert, moving around cage.
	29	am	Quiet but alert, sitting on ladder, liquid faeces.
		pm	Quiet but alert, normal faeces.
	30	am	Alert but sitting quietly in hammock, dry and loose faeces.
		pm	Alert, standing on ladder, reacts to external stimuli, very loose faeces.
	31	am	Animal found dead in cage.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y244F	1	am	Quiet but alert.
		pm	Quiet but alert.
	2	am	Quiet but alert, occasionally active.
		pm	Quiet but alert, occasionally active.
	3	am	Alert and reasonably active, itching wound.
		pm	Alert, gentle activity.
	4	am	Quiet and lying on perch, small swelling and scab above wound.
		pm	Active.
	5	am	Quiet but alert, active when approached, heavily menstrual.
		pm	Alert and active.
	6	am	Quiet, sitting on ladder, attempting to sleep, reacts to external stimuli.
		pm	Alert and fairly active.
	7	am	Quiet but alert, liquid faeces.
		pm	Quiet but alert, vocalisation when approached.
	8	am	Quiet but alert.
		pm	Quiet but alert.
	9	am	Quiet but alert, dark faeces.
		pm	Alert and active, dark faeces.
	10	am	Quiet but alert, occasionally active, dark faeces.
		pm	Alert and active, dark faeces.
	11	am	Quiet but alert, slightly active, dark faeces.
		pm	Quiet but alert, dark faeces.
	12	am	Quiet but alert, reasonably active, pale faeces.
		pm	Quiet but alert, active, sitting on ladder, dark faeces.
	13	am	Sitting on ladder, normal faeces.
		pm	Alert and active.
	14	am	Quiet but alert, active, standing on cage floor, dark faeces.
		pm	Alert, occasionally active, normal faeces.
	15	am	Alert, occasionally active, loose faeces.
		pm	Alert and active, loose faeces.
	16	am	Alert and fairly active, loose faeces.
		pm	Alert and active when stimulated.
	17	am	Quiet but alert, loose faeces.
		pm	Quiet but alert, occasionally active, normal faeces.
	18	am	Quiet but alert, slightly active, grooming self, dark faeces.
		pm	Alert and active, normal faeces.
	19	am	Quiet but alert, sitting on perch grooming self.
		pm	Quiet but alert, grooming self, dark faeces.
	20	am	Alert and active, normal faeces.
		pm	Alert and active, dark faeces.
	21	am	Quiet but alert, normal faeces.
		pm	Alert and active.
	22	am	Quiet but alert, sitting on perch, moves when approached.
		pm	Quiet but alert.
	23	am	Quiet but alert, reacts to external stimuli, liquid faeces.
		pm	Quiet and huddled at back of cage, reasonably alert, responds to external stimuli, liquid faeces.
	24	am	Alert, occasionally active, loose faeces.
		pm	Quiet but alert, sitting on ladder, loose faeces.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y244F (cont)	25	am	Alert, quiet, occasionally active, dark loose faeces.
		pm	Quiet but alert, dark loose faeces.
	26	am	Quiet but alert and active when stimulated, dark loose faeces.
		pm	Quiet but alert and active when stimulated.
	27	am	Quiet but alert, dark faeces.
		pm	Quiet but alert, dark faeces.
	28	am	Quiet but alert, sitting on ladder, normal faeces.
		pm	Quiet but alert, sitting on ladder.
	29	am	Quiet but alert, slightly active, loose faeces.
		pm	Alert and fairly active, normal faeces.
	30	am	Quiet but alert, loose/liquid faeces.
		pm	Alert and active, very loose faeces.
	31	am	Alert and fairly active, sitting on perch, normal faeces.
		pm	Alert, sitting on perch, loose faeces.
	32	am	Alert and responding to external stimuli, sitting on perch, loose faeces.
		pm	Quiet but alert when stimulated, normal faeces.
	33	am	Quiet and huddled, vocalisation, occasionally active, pelleted faeces.
		pm	Quiet and huddled at back of cage, pelleted faeces.
	34	am	Quiet and huddled, active when approached, loose faeces.
		pm	Quiet and huddled at back of cage, loose faeces.
	35	am	Quiet and huddled, reluctant to move, normal faeces.
		pm	Quiet but alert, loose faeces.
	36	am	Quiet but alert, little movement, normal faeces.
		pm	Quiet but alert, occasional activity, loose faeces.
	37	am	Quiet, very limited movement, very loose faeces.
		pm	Sacrificed for humane reasons.
Y246F	1	am	Quiet but alert.
		pm	Quiet but alert when approached, pelleted faeces.
	2	am	Quiet, sitting on ladder with eyes shut, alert when approached.
		pm	Quiet but alert.
	3	am	Quiet but alert, moves when approached, dark loose faeces.
		pm	Alert, gentle activity.
	4	am	Quiet but alert, occasionally active, dark faeces.
		pm	A little quieter than morning.
	5	am	Quiet but alert, sitting on ladder, occasionally lying down, active when approached, dark faeces.
		pm	Alert, sitting on perch, normal faeces.
	6	am	Quiet but alert, reacts to external stimuli, appears tired, sitting on perch leaning against ladder, dark faeces.
		pm	Quiet but alert, sitting on perch, normal faeces.
	7	am	Quiet but alert, dark faeces.
		pm	Quiet and huddled on perch, responds to stimuli but reluctant to move.
	8	am	Quiet but alert, dark faeces.
		pm	Quiet but alert when approached, dark faeces, tip of tail hard with discharge.
	9	am	Quiet, some reaction to external stimuli, vocalisation, loose faeces, vomit.
		pm	Quiet, head on ladder, not very responsive to stimuli, liquid faeces.
	10	am	Quiet but alert, occasionally active, vocalisation, liquid faeces.
		pm	Quiet but alert, dark faeces.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y246F (cont)	11	am	Quiet but alert, reacts to external stimuli, dark liquid faeces.
		pm	Quiet but alert, dark liquid faeces.
	12	am	Quiet but alert, huddled and reluctant to move, vocalising, dark liquid faeces.
		pm	Quiet but alert, reacts to external stimuli, reluctant to move, vocalising.
	13	am	Alert and active when stimulated, black loose faeces.
		pm	Alert and active when stimulated, normal faeces.
	14	am	Quiet and huddled, sitting on perch leaning against ladder, dark faeces.
		pm	Alert, occasionally active, normal faeces.
	15	am	Quiet but alert, sitting on ladder, dark faeces.
		pm	Quiet but alert, normal faeces.
	16	am	Quiet but alert when stimulated.
		pm	Quiet but alert, sometimes active.
	17	am	Quiet but alert when stimulated, dark loose faeces.
		pm	Quiet but alert when stimulated, loose faeces.
	18	am	Quiet but alert, slightly active, dark faeces.
		pm	Quiet but alert, sitting on ladder with unusual posture, normal faeces.
	19	am	Quiet but alert, sitting on ladder, loose faeces.
		pm	Alert and active, sitting on ladder, dark loose faeces.
	20	am	Alert and active, loose faeces.
		pm	Alert and active, dark loose faeces.
	21	am	Quiet but alert, active when stimulated, loose faeces.
		pm	Alert, some activity, loose faeces.
	22	am	Alert and fairly active, sitting on perch, loose faeces.
		pm	Alert and active, sitting on perch, dark loose faeces.
	23	am	Quiet but alert, reacts to external stimuli, sitting on ladder, loose faeces.
		pm	Quiet and huddled but alert.
	24	am	Alert, grooming self, dark loose faeces.
		pm	Quiet but alert, dark faeces.
	25	am	Quiet but alert, vocalising, loose faeces.
		pm	Quiet and huddled, alert when stimulated, normal faeces.
	26	am	Quiet but alert, sacrificed for humane reasons.
Y247M	1	am	Quiet, lying on cage floor, some activity seen during night, attempting to sleep, dark faeces.
		pm	Quiet but alert when approached, green vomit, dark faeces.
	2	am	Quiet but alert when stimulated, propped up against front of cage, dark faeces.
		pm	Quiet but alert and reasonably active, dark faeces.
	3	am	Quiet but alert, dark faeces.
		pm	Quiet but alert, dark faeces.
	4	am	Quiet but alert, reacts to external stimuli, slightly active, normal faeces.
		pm	Sitting on ladder, reluctant to move but alert.
	5	am	Quiet, sitting on ladder, huddled, reluctant to move, alert when stimulated.
		pm	Quiet but alert, dark faeces.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A11M	0	pm	Recovering from sedation, animal appears blind, no response to external stimuli, not focusing on a fixed point or sound, salivating profusely, unsteady and uncoordinated. Sacrificed for humane reasons.
Y248F	1	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert, sitting on perch, fruit vomit in tray.
	2	am	Quiet but alert when stimulated, yellow vomit in tray.
		pm	Quiet and huddled over ladder, alert when stimulated, loose faeces.
	3	am	Quiet but alert, lying on ladder, reluctant to move.
		pm	Quiet but alert, sitting on ladder, loose faces.
	4	am	Alert not very active, sitting on ladder, normal faeces.
		pm	Alert, sits on ladder, upright posture, moves if stimulated, gentle activity.
	5	am	Alert and occasionally active, sitting on ladder, responds to external stimuli, picking at wound, dark faeces.
		pm	Alert, sitting on perch, upright posture, looks bright, gentle activity, normal faeces.
	6	am	Quiet and huddled on perch, alert when approached.
		pm	Alert and occasionally active.
	7	am	Alert and active.
		pm	Quiet and huddled on ladder, unresponsive when approached.
	8	am	Alert, reasonably active.
		pm	Quiet and huddled on ladder, alert when stimulated.
	9	am	Quiet and huddled on ladder, alert when stimulated.
		pm	Quiet but alert.
	10	am	Alert and active, grooming self.
		pm	Alert and active.
	11	am	Alert and active, picking at wound.
		pm	Alert and occasionally active.
	12	am	Alert and active, moving around cage.
		pm	Quiet but alert, piloerection, huddled at times, loose liquid faeces.
	13	am	Alert and active, loose faeces.
		pm	Alert and active, loose faeces.
	14	am	Alert and active, sitting on cage floor, normal faeces.
		pm	Alert and active, sitting on ladder.
	15	am	Alert and active.
		pm	Alert and active.
	16	am	Alert and fairly active, picking at wound.
		pm	Alert and active.
	17	am	Alert and fairly active.
		pm	Alert and active.
	18	am	Alert and fairly active.
		pm	Quiet but alert, loose faeces.
	19	am	Quiet but alert, sitting on perch, normal faeces.
		pm	Quiet but alert
	20	am	Alert, occasionally active, dark faeces.
		pm	Alert and active, normal faeces.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y248F (cont)	21	am	Alert and reasonably active, pale faeces.
		pm	Quiet but alert, appears asleep, pale faeces.
	22	am	Bright and alert, sitting on perch, occasionally active, normal faeces.
		pm	Alert and active, pacing up and down perch.
	23	am	Bright, alert and active.
		pm	Bright, alert and active.
	24	am	Quiet but alert.
		pm	Alert and active, pacing around cage, soft faeces.
	25	am	Quiet but alert, occasionally active, soft faeces.
		pm	Alert and fairly active, loose faeces.
	26	am	Quiet but alert, sitting on ladder, soft faeces, vomit in tray.
		pm	Alert sitting on ladder, active when stimulated, loose faeces.
	27	am	Alert and fairly active, loose faeces.
		pm	Alert and fairly active, loose faeces.
	28	am	Alert and fairly active, liquid faeces.
		pm	Alert and active.
	29	am	Quiet but alert, liquid faeces.
		pm	Quiet but alert, liquid faeces.
	30	am	Quiet, liquid faeces.
		pm	Quiet but alert, pelleted faeces.
	31	am	Alert, sitting in hammock, moves when stimulated, pelleted and loose faeces.
		pm	Alert, sitting in hammock, not very active, loose faeces.
	32	am	Quiet but alert, moving around cage, loose faeces.
		pm	Quiet but alert, moves around cage when stimulated, loose faeces.
	33	am	Quiet but alert, moving around cage, loose faeces.
		pm	Quiet but alert, huddled on ladder, loose/liquid faeces.
	34	am	Quiet but alert, loose faeces.
		pm	Quiet but alert, active if stimulated.
	35	am	Quiet but alert if stimulated, sitting on perch, loose faeces.
		pm	Quiet but alert, responds when stimulated, liquid faeces.
	36	am	Quiet but alert, sitting on ladder, active when stimulated, pale loose faeces.
		pm	Quiet but alert.
	37	am	Quiet but alert, loose faeces.
		pm	Alert.
	38	am	Quiet but alert, moves when stimulated, loose faeces.
		pm	Alert, sitting on ladder, appears sleepy, loose faeces.
	39	am	Quiet but alert, resting on ladder, loose faeces.
		pm	Quiet but alert, small amount of activity, very loose faeces.
	40	am	Quiet and huddled but alert, sitting on ladder, reluctant to move, loose liquid faeces.
		pm	Grooming self, loose faeces.
	41	am	Quiet but alert, sitting on ladder, some activity, liquid faeces.
		pm	Quiet and huddled, sitting on perch, active when stimulated, loose faeces.
	42	am	Quiet but alert when stimulated, sitting on ladder, loose faeces.
		pm	Subdued and huddled, reacts to stimuli but reluctant to move, liquid faeces, grinding teeth.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day No.		Observation
Y248F (cont)	43	am	Quiet but alert, sitting on ladder, loose faeces.
		pm	Quiet but alert, loose faeces.
	44	am	Quiet but alert, sitting on ladder, active when stimulated, loose faeces.
		pm	Quiet but alert, active when stimulated, sitting on ladder grooming, patchy areas of bruising on back.
	45	am	Quiet and huddled over ladder, retching, salivating, little response to stimulation, liquid faeces.
		pm	Quit and huddled on ladder, alert when stimulated, loose faeces.
	46	am	Quiet but alert, huddled over ladder, "puffy" eyes and face, loose/liquid faeces.
		pm	Quiet but alert, sitting on ladder, normal faeces.
	47	am	Quiet and huddled, loose faeces.
		pm	Quiet and huddled, loose faeces.
	48	am	Vomiting, very quiet and subdued, head on ladder, not moving, body yellow in colour. Sacrificed for humane reasons.
A15M	1	am	Quiet but alert, reluctant to move.
		pm	Quiet but alert, occasionally active, sitting on cage floor.
	2	am	Quiet but alert, little movement.
		pm	Quiet but alert.
	3	am	Alert, little interest in surroundings.
		pm	Quiet but alert.
	4	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert.
	5	am	Quiet but alert, sitting on ladder.
		pm	Quiet but alert.
	6	am	Quiet but alert.
		pm	Quiet but alert, sitting at back of cage, poor appetite.
	7	am	Quiet but alert, sitting in corner of cage.
		pm	Quiet, lying on ladder, no interest in surroundings.
	8	am	Quiet but alert, occasionally active, black loose faeces, vomit in tray.
		pm	Quiet but alert, normal faeces.
	9	am	Quiet but alert, sitting in corner of cage, occasionally active.
		pm	Very subdued, eyes partially closed, eyes sunken, abdomen distended, reluctant to move, huddled posture. Sacrificed for humane reasons.

APPENDIX 11

Individual clinical signs

Explanatory notes

Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day, the signs are considered to be unrepresentative of the underlying condition of each animal.

Clinical signs are reported from the day following transplant (Day 1) except where the animal did not survive beyond Day 0.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y250f	1	am	Quiet but alert to external stimuli.
		pm	Quiet and huddled on cage floor, alert when stimulated.
	2	am	Quiet but alert when disturbed, vomit in cage, loose faeces.
		pm	Quiet and huddled, sitting on perch, alert when stimulated, normal faeces.
	3	am	Quiet but alert, sitting on hammock, appears subdued.
		pm	Quiet and huddled, becomes alert for a short time when stimulated. Sedated for necropsy.
Y155m	1	am	Bright and alert to external stimuli – occasionally active.
		pm	Quiet but alert.
	2	am	Bright and alert, quiet, active, moving around cage, vomit in cage.
		pm	Quiet but alert, active when stimulated.
	3	am	Quiet but alert, active when stimulated, vomit in cage.
		pm	Quiet but alert, sitting upright.
	4	am	Quiet but alert, huddled in corner of cage, grooming occasionally. Swelling around eyes. Hunched when moving around cage but only when stimulated. Vomit in cage. Later; quiet and sitting on ladder, eyes closed, minimal reaction to external stimuli. Swelling around eyes. Sedated for necropsy. .
A14f	0	pm	Died.
A94m	1	am	Alert, sitting on perch, periods of activity around cage and periods of subdued behaviour.
		pm	Quiet, sitting on perch, subdued, does not appear to want to move.
	2	am	Quiet but alert, reluctant to move.
		pm	Quiet, eyes closed, sitting on cage floor, reluctant to move, minimal response to stimulation. Sedated for necropsy.
Y168f	1	am	Subdued, lying on ladder, aggressive when approached.
		pm	Alert, sitting on perch, moving around slowly, resting on ladder hunched.
	2	am	Quiet but alert, vomit in cage.
		pm	Quiet, huddled, head between legs, little/no movement, later – quiet but alert.
	3	am	Quiet but alert, occasional activity.
		pm	Quiet but alert to external stimuli, occasionally moving around cage..
	4	am	Alert, sitting on ladder, vomit in cage, loose and dark discoloured faeces.
		pm	Alert and quite active..
	5	am	Quiet but alert, aggressive when stimulated, sitting on cage floor. Normal faeces.
		pm	Quiet but alert, sitting on perch with pairing partner.
	6	am	Quiet but alert, active when stimulated, sitting on drip catcher. Loose/liquid faeces.
		pm	Quiet but alert, sitting on hammock, huddled, some reaction to external stimuli. Very loose faeces.
	7	am	Quiet but alert, moving around cage. Loose faeces.
		pm	Bright and alert, occasionally moving around cage, soft faeces.
	8	am	Quiet but alert. Loose faeces.
		pm	Alert and active, grooming pairing partner. Normal faeces.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y168f	9	am	Alert and active, pacing around cage and ladder.
		pm	Alert and active, grooming pairing partner.
	10	am	Alert and active.
		pm	Alert and active.
	11	am	Quiet but alert. Slightly active, standing on ladder.
		pm	Bright and alert, occasionally active. Later – quiet, huddled.
	12	am	Alert but quiet, moving around cage.
		pm	Quiet and huddled with eyes shut, on ladder.
	13	am	Alert but quiet/moving around cage.
		pm	Quiet but alert, sitting on ladder. Dark faeces.
	14	am	Alert and active, grooming, moving around cage. Normal faeces.
		pm	Quiet but alert, sitting on perch.
	15	am	Bright and alert to external stimuli, sitting on ladder.
		pm	Quiet but alert, sitting on ladder, active/aggressive when stimulated.
	16	am	Alert, active when stimulated, perched on ladder.
		pm	Quiet but alert, sitting on ladder, huddled.
	17	am	Quiet but alert, active/aggressive when stimulated.
		pm	Alert and active.
	18	am	Quiet but alert, sitting on perch, active when stimulated.
		pm	Grooming with pairing partner.
	19	am	Quiet but alert, active when stimulated.
		pm	Quiet but alert, cuddling pairing partner, appears drowsy.
	20	am	Quiet but alert, aggressive when approached, sitting on ladder facing rear of cage.
		pm	Quiet but alert, sitting on ladder. Loose faces.
	21	am	Animal appears to be resting, lying on ladder, reacts to external stimuli. Very loose faeces.
		pm	Alert and active, sitting on perch. Lose faeces.
	22	am	Quiet and huddled on perch, reluctant to move even if stimulated. Pale loose faeces and dark liquid faeces.
		pm	Quiet but alert, sitting on ladder with pairing partner, quite active when stimulated. Liquid faeces.
	23	am	Quiet and huddled, sitting on top of ladder, non-responsive to stimulation, small body tremors. Liquid faeces. Sacrificed for humane reasons.

APPENDIX 11

Individual clinical signs

Explanatory notes

1. Only first and last observations of the day are reported. Due to manipulations/investigations performed on animals during the day, the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1).

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A98f	1	am	Bright and alert to external stimuli – occasionally active, blood in tray.
		pm	Alert and aggressive, sitting on perch, blood in tray.
	2	am	Alert, reluctant to move from sitting on perch, becoming aggressive when stimulated.
		pm	Quiet but alert, sitting on perch.
	3	am	Quiet but alert, becoming aggressive when stimulated.
		pm	Quiet but alert.
	4	am	Alert and occasionally active.
		pm	Quiet, not very alert, although active when stimulated.
	5	am	Quiet but alert, some activity when disturbed.
		pm	Quiet and huddled but alert, reacts to external stimuli with slight activity.
	6	am	Underactive, slightly subdued, does not use the perch, reacts positively when provoked. Sedated for sacrifice.
A81m	1	am	Alert and active.
		pm	Quiet but alert, huddled on ladder.
	2	am	Appears alert and fairly active, moving around cage.
		pm	Quiet but alert, sitting on ladder, active when stimulated, unusual posture on ladder.
	3	am	Quiet but alert, lying on ladder, active when stimulated. Vomit on perch.
		pm	Quiet but alert, quite active.
	4	am	Quiet but alert, straining to pass urine.
		pm	Quiet but alert, sitting on ladder, active when stimulated. Vomit in cage.
	5	am	Alert and fairly active
		pm	Animal on perch with eyes shut, quiet, huddled.
	6	am	Quiet but alert, sitting on perch, active and aggressive when stimulated.
		pm	Subdued and huddled, appears asleep, reluctant to move when stimulated. Straining to pass urine.
	7	am	Alert, sitting on ladder, gentle activity.
		pm	Quiet but alert, quite active when stimulated, straining to urinate.
	8	am	Quiet but alert, sitting on perch, becoming aggressive when observed. Scrotum appears swollen.
		pm	Quiet but alert, sitting upright, occasionally active.
	9	am	Gentle activity, puffy under eyes, some swelling lower abdomen, scrotum swollen.
		pm	Quiet and huddled over ladder, alert when stimulated.
	10	am	Alert, gentle activity – aggressive. Slightly puffy under eyes.
		pm	Quiet but alert, huddled on perch, eyes shut, appears tired.
	11	am	Alert, huddled on perch, some activity.
		pm	Quiet and huddled, moves when stimulated.
	12	am	Quiet and huddled, sitting on ladder, alert and aggressive.
		pm	Quiet and huddled but alert. Loose faeces.
	13	am	Quiet but alert, sitting on ladder, straining to urinate, vocal. Soft grey faeces.
		pm	Quiet, huddled. Loose faeces.
	14	am	Alert, gentle activity, swelling of scrotum.
		pm	Quiet but alert. Normal faeces.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A81m (cont)	15	am	Quiet but alert, sitting on ladder, active when stimulated.
		pm	Quiet but alert, grooming partner.
	16	am	Quiet but alert, sitting on ladder, slightly huddled, quite active when stimulated.
		pm	Quiet and huddled with pairing partner, alert when stimulated.
	17	am	Quiet but alert, sitting on ladder, huddled, alert and aggressive to stimulation.
		pm	Quiet but alert, sitting on ladder.
	18	am	Quiet but alert, sitting on ladder.
		pm	Quiet but alert.
	19	am	Alert and gentle activity. Slightly puffy under eyes. Loose faeces.
		pm	Quiet but alert, active if stimulated. Dark loose faeces.
	20	am	Quiet but alert, slightly huddled posture, little movement. Normal faeces.
		pm	Alert and active when stimulated.
	21	am	Quiet but alert, slightly huddled posture, active when stimulated.
		pm	Quiet but alert.
	22	am	Quiet but alert, huddled on ladder.
		pm	Quiet and huddled, abdomen appears distended, breathing appears faster than normal..
	23	am	Quiet but alert, puffy eyelids.
		pm	Quiet but alert, little activity until stimulated, mainly sitting on ladder.
	24	am	Quiet but alert, lying on ladder.
		pm	Quiet and huddled on perch, alert when stimulated.
			Signs prior to sacrifice – very subdued, breathing rate in excess of 80 breaths per minute, breathing audible, reluctant to move, abdomen very distended. Sacrificed for humane reasons.
A92m	1	am	Resting, lying on bottom of cage, appears alert when stimulated, small movements observed, appears drowsy.
		pm	Lying prostrate on fleece, no activity, minimal head movement, eyes more open than previously. No response when touched, eyes closing and very weak. Sacrificed for humane reasons.
Y153m	1	am	Quiet but alert, sitting on ladder, occasionally moving around cage.
		pm	Quiet but alert, sitting on ladder, some activity.
	2	am	Alert and quite active, pacing up and down ladder and perch. Vomit in tray. Loose faeces.
		pm	Alert and active sitting on ladder. Loose faeces.
	3	am	Quiet but alert, moves if stimulated. Loose faeces.
		pm	Alert, gentle activity. Lose faeces.
	4	am	Quiet but alert, sitting on ladder, vomit in tray. Loose faeces.
		pm	Quiet but alert, sitting on perch, appears lethargic when moving. Loose faeces. Sedated for sacrifice.
A97m	1	am	Huddled on perch, appears asleep, observed straining.
		pm	Quiet but alert, sitting on perch, some activity.
	2	am	Quiet but alert, sitting on ladder, grooming.
		pm	Quiet but alert, sitting on ladder, occasionally active.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A97m (cont)	3	am	Quiet but alert, occasionally active.
		pm	Alert and quite active, blood in cage.
	4	am	Alert, sitting on ladder.
		pm	Quiet, on perch, occasionally active.
	5	am	Quiet but alert, sitting on perch, active and vocal when stimulated.
		pm	Alert, occasionally active.
	6	am	Alert and active while observed. Some swelling lower abdomen.
		pm	Alert, occasionally active.
	7	am	Quiet but alert, sitting on perch, little activity.
		pm	Alert and active.
	8	am	Alert and active. Some swelling lower abdomen. Loose faeces.
		pm	Alert and active. Loose faeces.
	9	am	Alert and active, sitting on perch in top cage. Some swelling lower abdomen. Loose faeces.
		pm	Alert, huddled, lipsmacking.
	10	am	Alert and active, sitting on perch
		pm	Alert and active.
	11	am	Alert and active. Normal faeces.
		pm	Quiet but alert.
	12	am	Quiet but alert, sitting on perch, slightly active..
		pm	Quiet but alert, sitting on perch, occasional movement. Grey faeces.
	13	am	Alert , active and friendly. Some swelling lower abdomen. Normal faeces.
		pm	Alert, fairly active.
	14	am	Quiet but alert, sitting on perch, slightly active.
		pm	Subdued and huddled, reluctant to move when stimulated, slight body tremors. Swelling around both eyes, fluid collection around wound.
	15	am	Quiet but alert, huddled on perch, no movement unless stimulated. Pelleted faeces.
		pm	Quiet but alert, sitting on perch, active when stimulated. Normal faeces.
	16	am	Quiet and huddled, sitting on perch, unresponsive to simuli, puffy eyes and pallor. Bruising on legs. Sacrificed for humane reasons.
A87m	1	am	Quiet but alert, lying on cage floor or perch, little activity..
		pm	Quiet but alert, sitting on ladder, reluctant to move.
	2	am	Generally quiet, gentle activity, slightly puffy under eyes. Loose faeces..
		pm	Quiet and huddled on perch, alert when stimulated.
	3	am	Generally quiet, gentle activity, alert. Sacrificed for humane reasons.
A87m	1	am	Quiet, occasional gentle activity, sits on perch.
		pm	Quiet and huddled.
	2	am	Alert but generally quiet, reduced activity.
		pm	Quiet, sitting at back of cage on floor.
	3	am	Alert, some activity, slightly huddled when still.
		pm	Subdued and huddled, sitting on cage floor, reluctant to move when stimulated. Sedated for sacrifice.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y149m	1	am	Very quiet/subdued, huddled on perch, little movement, no movement when approached.
		pm	Quiet, huddled, little response to stimuli.
	2	am	Quiet but alert, sitting on ladder, unresponsive to stimuli.
		pm	Signs noted prior to sacrifice – very quiet/subdued, huddled on perch, reluctant to move when stimulated. Sacrificed for humane reasons.
A84f	1	am	Alert, little movement, huddled on ladder, quiet, slightly subdued.
		pm	Quiet but alert, active when stimulated.
	2	am	Quiet but alert, sleeping on ladder, responsive to stimuli. Blood on tray.
		pm	Quiet and huddled on perch.
	3	am	Quiet but alert, lying on ladder, moving around if stimulated.
		pm	Signs noted prior to sacrifice – subdued, huddled on cage floor. Sacrificed for humane reasons.
A85m	1	am	Quiet but alert, active when stimulated, sitting on cage floor.
		pm	Quiet but alert if stimulated, lying on perch.
	2	am	Quiet but alert, moves around cage when stimulated
		pm	Quiet and huddled over ladder, alert when stimulated.
	3	am	Alert, active when stimulated, sitting on ladder.
		pm	Alert and sitting on floor, occasionally active.
	4	am	Alert, slightly huddled, some movement.
		pm	Alert, moving around cage when stimulated.
	5	am	Quiet but alert, sitting upright, active when stimulated.
		pm	Quiet but alert.
	6	am	Quiet but alert, active when stimulated.
		pm	Quiet but alert, sitting on perch, grooming pairing partner, active when stimulated.
	7	am	Quiet but alert, active when disturbed.
		pm	Alert, some activity with pairing partner, grooming same. Loose faeces.
	8	am	Alert, occasionally active, slightly huddled. Loose faeces.
		pm	Quiet and alert, occasional activity. Liquid faeces.
	9	am	Quiet but alert, sitting on perch, active when stimulated. Loose Faeces.
		pm	Alert, some activity. Loose faeces.
	10	am	Alert, moving around cage, active. Vomit in cage. Loose faeces.
		pm	Quiet but alert.
	11	am	Alert, active, moving around cage when stimulated. Lose faeces.
		pm	Alert, active.
	12	am	Alert, active when stimulated. Loose faeces.
		pm	Quiet but alert.
	13	am	Quiet but alert, sitting on cage floor. Loose faeces.
		pm	Alert, some movement around cage, grooming pairing partner.
	14	am	Subdued and hulled, vocalising, reluctant to move when stimulated. Appears weak and unsteady. Scrotum and abdomen appear swollen. Liquid faeces. Sacrificed for humane reasons.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A79m	1	am	Quiet but alert.
		pm	Quiet but alert, active when stimulated, vocal to outside noise.
	2	am	Quiet but alert, little activity when disturbed.
		pm	Alert, occasionally active, slightly huddled and scratching.
	3	am	Quiet but alert, active when stimulated.
		pm	Alert, some activity.
	4	am	Alert and quite active, walking around perch and ladder. Pelleted faeces..
		pm	Quiet but alert. Normal faeces.
	5	am	Quiet but alert, sitting on ladder. Pelleted faeces.
		pm	Quiet but alert.
	6	am	Alert, sitting on ladder, moves when stimulated. Pelleted faeces.
		pm	Quiet but alert.
	7	am	Alert, sitting on ladder, active when stimulated. Pelleted faeces.
		pm	Alert and active.
	8	am	Alert and active, straining to pass urine. Normal faeces.
		pm	Alert, huddled on ladder, little movement.
	9	am	Quiet but alert, sitting on perch, active and vocal when stimulated, straining to pass urine.
		pm	Alert and active, moving from cage to cage, picking at scar.
	10	am	Quiet and huddled, becomes alert when stimulated, straining to pass urine. Loose faeces.
		pm	Quiet and huddled with pairing partner. Normal faeces.
	11	am	Alert and vocalising, sitting upright on perch. Loose faeces.
		pm	Quiet but alert. Loose faeces.
	12	am	Quiet but alert. Loose faeces.
		pm	Quiet , huddled, alert when stimulated.
	13	am	Quiet but alert, sitting on cage floor, active when stimulated. Loose faeces.
		pm	Quiet but alert. Loose faeces.
	14	am	Quiet but alert, sitting on ladder. Loose faeces.
		pm	Alert and active.
	15	am	Alert and quite active. Grey faeces.
		pm	Alert and active.
	16	am	Quiet but alert, sitting on top of ladder, slightly active. Grey faeces.
		pm	Quiet and huddled.
	17	am	Alert, active, moving around cage. Pale faeces.
		pm	Alert and active.
	18	am	Alert, active, moving around cage. Normal faeces.
		pm	Alert and active.
	19	am	Alert, moving around cage.
		pm	Alert, slightly active.
	20	am	Bright, active and alert, vocalising.
		pm	Alert and active.
	21	am	Bright and alert, sitting on ladder. Loose faeces.
		pm	Quiet, Huddled.
	22	am	Alert and active, moving around cage. Normal faeces.
		pm	Alert and active, grooming with pairing partner.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A79m (cont)	23	am	Alert and active, moving around cage.
		pm	Alert and active, grooming pairing partner.
	24	am	Quiet but alert, slightly active.
		pm	Alert, slightly active.
	25	am	Alert and active.
		pm	Alert and active.
	26	am	Alert and active. Pale faeces.
		pm	Quiet but alert, some movement, sitting on ladder grooming self.
	27	am	Quiet but alert, lying on ladder, active when stimulated.
		pm	Quiet and huddled, sitting on perch, active when stimulated.
	28	am	Quiet but alert, sitting on ladder.
		pm	Alert and active, slightly huddled when still.
	29	am	Bright and alert, sitting on perch.
		pm	Alert, sits in sling, gentle activity if approached.
	30	am	Bright, alert, sitting in hammock.
		pm	Alert, slightly active. Loose dark faeces.
	31	am	Alert and active, slightly puffy around eyes.
		pm	Alert but sits quietly in sling. Normal faeces.
	32	am	Alert and active.
		pm	Quiet but alert, some activity.
	33	am	Quiet and huddled on perch but alert to external stimuli, eyes and face appear puffy.
		pm	Quiet but alert, active when stimulated.
	34	am	Alert, fairly active.
		pm	Alert, occasional activity, slightly puffy around eyes.
	35	am	Alert when stimulated, sitting on ladder. Pelleted faeces.
		pm	Quiet but alert.
	36	am	Quiet but alert, puffy around eyes. Normal faeces.
		pm	Quiet but alert. Liquid faeces.
	37	am	Quiet and huddled on ladder, responds to external stimuli, eyes and face appear puffy. Liquid faeces.
		pm	Quiet but alert.
	38	am	Quiet but alert, vomit in tray. Loose/liquid faeces.
		pm	Quiet but alert and huddled, slightly puffy around eyes. Loose/liquid faeces.
	39	am	Quiet and huddled, alert if stimulated. Slightly puffy around eyes. Loose/liquid faeces.
		pm	Quiet and huddled, responds to external stimuli, slightly puffy around eyes. Liquid faeces.
	40	am	Quiet but alert, slightly puffy around eyes. Loose/liquid faeces.
		pm	Quiet and huddled, alert when stimulated.
	41	am	Quiet, distended abdomen. Signs prior to sacrifice – subdued, reluctant to move. Sacrificed for humane reasons.
A88f	1	am	Very quiet, little activity.
		pm	Quiet but alert.
	2	am	Quiet but alert, active when disturbed.
		pm	Quiet but alert, lying on ladder, huddled, active when stimulated.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A88f (cont)	3	am	Quiet but alert, lying on ladder, moves when stimulated.
		pm	Quiet but alert, sitting on perch.
	4	am	Quiet but alert, aggressive, sitting on ladder.
		pm	Quiet but alert, occasional activity.
	5	am	Quiet but alert, aggressive, sitting on perch.
		pm	Alert and active.
	6	am	Alert and active when stimulated.
		pm	Quiet and huddled.
	7	am	Alert, active when stimulated. Pelleted faeces.
		pm	Alert, sitting on ladder, some movement when stimulated.
	8	am	Quiet but alert, lying on ladder, aggressive when stimulated. Loose faeces.
		pm	Alert, sitting on ladder, some movement when stimulated. Loose faeces.
	9	am	Quiet but alert, sitting on ladder, aggressive when stimulated. Normal faeces.
		pm	Alert and active.
	10	am	Quiet but alert, picking at wound, moves when stimulated.
		pm	Alert.
	11	am	Quiet but alert, slightly huddled posture on ladder.
		pm	Alert and active.
	12	am	Quiet but alert, sitting on ladder, aggressive when stimulated.
		pm	Alert and fairly active.
	13	am	Quiet but alert, sitting on ladder, active/aggressive when stimulated.
		pm	Quiet but alert.
	14	am	Quiet but alert, sitting on ladder, aggressive when stimulated.
		pm	Alert and alert.
	15	am	Alert and aggressive, sitting on perch.
		pm	Alert and active.
	16	am	Quiet but alert, occasionally active, sitting on perch. Dark faeces.
		pm	Quiet but alert.
	17	am	Alert, moves around cage when stimulated. Normal faeces.
		pm	Alert, sitting on ladder.
	18	am	Quiet but alert.
		pm	Quiet but alert.
	19	am	Quiet but alert, lying on ladder.
		pm	Quiet but alert, inactivity.
	20	am	Bright, alert and active.
		pm	Quiet and huddled, sitting on perch, alert and active when stimulated.
	21	am	Bright, alert, sitting on ladder.
		pm	Quiet, huddled.
	22	am	Alert, sitting on ladder.
		pm	Quiet and huddled, sitting on ladder, alert and aggressive when stimulated.
	23	am	Alert, active. Loose faeces.
		pm	Alert and active, grooming self.
	24	am	Quiet but alert, huddled on ladder, sitting grooming self.
		pm	Alert and active, playing with pairing partner.
	25	am	Quiet but alert. Dark loose faeces.
		pm	Quiet but alert on ladder, gentle activity if stimulated. Loose faeces.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A88f (cont)	26	am	Quiet but alert. Dark loose faeces.
		pm	Alert, some activity, sitting on ladder. Normal faeces.
	27	am	Quiet but alert, sitting on ladder, aggressive when stimulated.
		pm	Quiet but alert, aggressive when stimulated. Vomit during dose.
	28	am	Quiet but alert, lying on ladder.
		pm	Signs prior to sacrifice – quiet and huddled, unresponsive to stimuli, quiet but alert. Sacrificed for humane reasons.
A83m	1	am	Quiet but alert, little activity, occasionally closing eyes.
		pm	Alert, slight activity when stimulated, often lying on cage floor.
	2	am	Alert, some activity, sitting on ladder.
		pm	Alert, fairly active.
	3	am	Quiet but alert, sitting on ladder, active/aggressive when stimulated.
		pm	Quiet but alert.
	4	am	Quiet but alert, sitting on ladder.
		pm	Alert.
	5	am	Alert, active.
		pm	Quiet but alert.
	6	am	Alert, sitting on perch.
		pm	Quiet but alert.
	7	am	Quiet and huddled on ladder, active and vocal to stimulated.
		pm	Alert and active.
	8	am	Quiet but alert, sitting in corner of cage, aggressive when stimulated.
		pm	Alert and active. Liquid faeces.
	9	am	Quiet and huddled, becomes alert when stimulated, reluctant to move.
		pm	Alert.
	10	am	Quiet but alert, sitting on perch, weepy eyes. Loose faeces.
		pm	Quiet and huddled.
	11	am	Quiet and huddled in corner of cage, alert/active when stimulated. Normal faeces.
		pm	Quiet and huddled.
	12	am	Quiet but alert, huddled on floor.
		pm	Quiet, huddled, alert when stimulated.
	13	am	Quiet but huddled, alert if stimulated. Pale faeces.
			Signs noted prior to sacrifice – Huddled, subdued, slight tremors, unresponsive to stimuli. Sacrificed for humane reasons.
A86f	1	am	Quiet but alert, sitting on perch.
		pm	Quiet but alert, sitting on ladder.
	2	am	Alert and active, grooming self.
		pm	Alert.
	3	am	Quiet but alert, sitting on ladder, moves if stimulated.
		pm	Alert.
	4	am	Alert, some activity, sitting on ladder.
		pm	Alert and active.
	5	am	Alert and active, walking around cage.
		pm	Quiet but alert, some activity.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A86f (cont)	6	am	Quiet but alert, aggressive when stimulated.
		pm	Alert, active, grooming self.
	7	am	Quiet but alert when stimulated.
		pm	Alert and active, moving around freely.
	8	am	Quiet but alert, sitting on perch, quite active.
		pm	Quiet but alert.
	9	am	Quiet but alert, slightly active, sitting on perch. Dark faeces.
		pm	Alert, active.
	10	am	Alert, moving around cage. Normal faeces.
		pm	Alert and active.
	11	am	Alert and active.
		pm	Alert and active.
	12	am	Alert and active.
		pm	Quiet but alert, grooming self.
	13	am	Bright and alert, moving freely around cage.
		pm	Quiet and huddled with pairing partner.
	14	am	Bright and alert.
		pm	Quiet, huddled.
	15	am	Alert, sitting on ladder.
		pm	Alert and active, play-fighting and grooming pairing partner.
	16	am	Alert, active when stimulated.
		pm	Alert and active, grooming pairing partner.
	17	am	Bright and alert, grooming self on ladder.
		pm	Bright and alert, foraging in tray.
	18	am	Bright and alert, active.
		pm	Quiet, occasionally gentle activity, sitting on shelf.
	19	am	Bright and alert, moving around cage.
		pm	Alert and active.
	20	am	Alert and active, moving around cage.
		pm	Alert and active.
	21	am	Quiet but alert, active when stimulated.
		pm	Alert and active.
	22	am	Bright and alert, occasionally active.
		pm	Alert, gentle activity.
	23	am	Bright and alert, very active.
		pm	Quiet but alert.
	24	am	Quiet but alert, sitting on perch.
		pm	Alert, gentle activity.
	25	am	Alert and active. Pelleted faeces.
		pm	Alert, some activity.
	26	am	Bright, alert, active around cage.
		pm	Quiet but active when stimulated, sitting with pairing partner.
	27	am	Alert and fairly active.
		pm	Alert and active.
	28	am	Alert, bright, active.
		pm	Quiet but alert, grooming self.
	29	am	Quiet but alert.
		pm	Quiet but alert.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A86f (cont)	30	am	Bright and alert, grooming self, occasionally active.
		pm	Alert. Pelleted faeces.
	31	am	Quiet but alert. Loose faeces.
		pm	Alert, gentle activity. Normal faeces.
	32	am	Quiet but alert, some activity. Loose faeces.
		pm	Alert, fairly active. Loose faeces.
	33	am	Alert, grooming self. Loose faeces.
		pm	Alert, active, vocalising.
	34	am	Quiet and huddled. Normal faeces.
		pm	Quiet, resting in hammock.
	35	am	Quiet but alert.
		pm	Alert, some activity
	36	am	Alert, gentle activity. Loose faeces.
		pm	Quiet but alert, active when stimulated.
	37	am	Alert and active. Pale loose/liquid faeces.
		pm	Alert and fairly active. Playing.
	38	am	Alert, reluctant to move when stimulated. Pale loose faeces.
		pm	Alert and active, huddled when still.
	39	am	Alert and active. Loose faeces.
		pm	Alert. Loose faeces.
	40	am	Alert, active when stimulated, occasionally huddled. Loose/liquid faeces.
		pm	Active when stimulated. Loose faeces.
	41	am	Alert, gentle activity, vocal. Loose faeces.
		pm	Alert, gentle activity.
	42	am	Alert, some activity. Loose faeces.
		pm	Quiet but alert, active when stimulated.
	43	am	Alert, gentle activity, puffy around eyes. Normal faeces.
		pm	Alert, vocalising.
	44	am	Quiet but alert, huddled on ladder, fluid around eyes.
		pm	Alert, slightly huddled, puffy eyes. Loose faeces.
	45	am	Quiet but alert when stimulated.
		pm	Alert and active.
	46	am	Alert and active, sitting on perch, occasionally moving around cage. Loose faeces.
		pm	Alert, gentle activity.
	47	am	Quiet but alert, sitting on ladder. Normal faeces.
		pm	Quiet but alert, active when stimulated.
	48	am	Quiet and huddled, becomes alert for short periods when stimulated, grinding teeth..
		pm	Alert, active.
	49	am	Alert and active, puffy around eyes. Loose faeces.
		pm	Alert on ladder, gentle activity, puffy around eyes. Loose faeces.
	50	am	Alert, sitting on ladder grinding teeth, active and aggressive when stimulated. Loose faeces.
		pm	Alert, puffy around eyes. Dark loose/liquid faeces.
	51	am	Alert and active, puffy around eyes. Loose faeces.
		pm	Quiet but alert, occasionally active. Loose/liquid faeces.
	52	am	Quiet but alert. Loose faeces.
		pm	Signs noted prior to sacrifice – collapsed on cage floor, attempting to get up, very unsteady. Sacrificed for humane reasons.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y147m	1	am	Quiet but alert, sitting on ladder, reluctant to move.
		pm	Alert in cage.
	2	am	Quiet but alert, active when stimulated
		pm	Alert and active.
	3	am	Quiet but alert, moving around cage.
		pm	Alert, active.
	4	am	Alert, active when stimulated.
		pm	Alert, active.
	5	am	Alert, sitting on ladder.
		pm	Quiet but alert, sitting on ladder, active when stimulated.
	6	am	Alert, sitting on ladder.
		pm	Quiet and huddled.
	7	am	Alert, active, moving around cage.
		pm	Quiet but alert, lying on ladder, active when stimulated.
	8	am	Active and alert, sitting on ladder.
		pm	Quiet but alert, lying on ladder, aggressive when approached.
	9	am	Alert and active, aggressive when approached.
		pm	Quiet but alert, active and aggressive when approached. Dark faeces.
	10	am	Quiet but alert, active when stimulated. Pelleted faeces.
		pm	Alert and active.
	11	am	Quiet but alert, sitting on ladder. Normal faeces.
		pm	Quiet but alert, sitting on ladder.
	12	am	Quiet but alert, sitting on perch, active and aggressive when approached.
		pm	Quiet but alert, grooming with pairing partner.
	13	am	Quiet but alert, active when stimulated.
		pm	Alert and active.
	14	am	Quiet but alert, sitting in hammock.
		pm	Quiet, sitting on ladder, huddled, becomes active if stimulated.
	15	am	Quiet but alert, lying in hammock.
		pm	Quiet but alert, aggressive when stimulated.
	16	am	Alert, aggressive, siting in hammock, puffy around eyes.
		pm	Quiet and huddled in hammock, alert when stimulated.
	17	am	Alert, sitting in hammock. Loose faeces.
		pm	Alert, occasional activity.
	18	am	Bright, alert and active. Loose/liquid faeces.
		pm	Quiet, alert, moving around with pairing partners.
	19	am	Quiet, sitting in hammock, alert when stimulated. Loose/liquid faeces.
		pm	Quiet and huddled, puffy around eyes and face. Dark liquid faeces.
	20	am	Very quiet and subdued, sitting on hammock with head down, face very puffy, reluctant to move when stimulated. Liquid faeces. Sacrificed for humane reasons.
A80f	1	am	Quiet but alert, huddled on ladder.
		pm	Alert in cage, moving around.
	2	am	Quiet but alert, moving around cage
		pm	Quiet but alert.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A80f (cont)	3	am	Quiet but alert, active when stimulated.
		pm	Alert and active.
	4	am	Alert, moving around cage.
		pm	Quiet and alert.
	5	am	Quiet and huddled on ladder.
		pm	Quiet but alert, sitting on perch.
	6	am	Quiet but alert. Loose faeces.
		pm	Quiet and huddled.
	7	am	Quiet but alert, sitting on perch, leaning on ladder. Loose faeces
		pm	Signs prior to sacrifice – subdued and huddled, resting against wall of cage, appears sleepy. Abdomen appears distended. Reluctant to move when stimulated. Little reaction to stimuli. Sacrificed for humane reasons.
A82f	1	am	Quiet but alert, sitting on perch, leaning against cage.
		pm	Quiet and huddled, active when stimulated.
	2	am	Quiet but alert when stimulated.
			Signs prior to sacrifice – lying on cage floor, unresponsive to stimulation. Sacrificed for humane reasons.
Y143m	1	am	Alert, sitting on perch.
		pm	Quiet and huddled, sitting in corner of cage, alert when stimulated.
	2	am	Quiet, no movement when stimulated, leaning on cage door, eyes partially closed.
		pm	Signs prior to sacrifice – Unaware of surroundings, sitting upright, very quiet, minimal response to stimulation. Sacrificed for humane reasons.
A90m	1	am	Alert, active when stimulated, aggressive to observer.
		pm	Quiet but alert, lying on ladder, aggressive when stimulated.
	2	am	Alert when stimulated, reluctant to move. Vomit in cage..
		pm	Quiet but alert.
	3	am	Quiet but alert, scratching, fluid build-up in abdomen, grooming self.
		pm	Quiet but alert, huddled, aggressive when approached. Vomit in cage.
	4	am	Quiet but alert, sitting on ladder, aggressive when approached.
		pm	Quiet but alert, sitting on ladder, gentle activity if stimulated.
	5	am	Quiet but alert, sitting on ladder, aggressive when approached.
		pm	Alert and active on ladder.
	6	am	Quiet and huddled, sitting on ladder, active and aggressive when stimulated.
		pm	Quiet but alert, sitting on perch.
	7	am	Alert and aggressive.
		pm	Alert and active, vocalising, occasionally lying on hammock.
	8	am	Quiet but alert if stimulated, sitting in hammock. Pale faeces.
		pm	Quiet but alert, sitting in hammock, occasionally huddled. Normal faeces.
	9	am	Alert, sitting in hammock.
		pm	Quiet but alert, sitting on perch.
	10	am	Quiet but alert, sitting in hammock.
		pm	Quiet but alert, huddled on perch.
	11	am	Quiet but alert, huddled on ladder, active and aggressive when stimulated.
		pm	Quiet and huddled, alert when stimulated.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A90m (cont)	12	am	Quiet, huddled on ladder, alert if stimulated, but resumes huddled posture.
		pm	Quiet and huddled on ladder, minimal response when stimulated.
	13	am	Quiet and huddled in hammock, little response to stimuli. Sacrificed for humane reasons.
Y170f	1	am	Quiet, some movement when stimulated.
		pm	Quiet and huddled, sitting in corner of cage, active when stimulated. Vomit in tray.
	2	am	Quiet and active when stimulated. Vomit in tray. Pelleted faeces
		pm	Quiet, reacts to external stimuli. Pelleted faeces.
	3	am	Quiet but alert, sitting on cage floor, aggressive when approached. Pelleted faeces.
		pm	Signs prior to sacrifice – subdued, eyes closed, lying across ladder, reluctant to move even when stimulated. Sacrificed for humane reasons.
A91m	1	am	Quiet moving around cage.
		pm	Quiet and huddled on ladder, alert when stimulated. Liquid faeces.
	2	am	Alert, sitting on ladder, gentle activity when stimulated. Loose/liquid faeces.
		pm	Alert, quiet and huddled on perch.
	3	am	Alert, sitting on perch.
		pm	Quiet and huddled in corner of cage, little response to stimuli.
	4	am	Lying on cage floor, appears weak when trying to sit up. Swollen abdomen, bruising to whole body including head and face, pale gums with bruising. Liquid faeces. . Sacrificed for humane reasons.
A164m	1	am	Quiet but alert, lying on ladder, moves if stimulated.
		pm	Quiet but alert, sitting on ladder.
	2	am	Quiet but alert, sitting on ladder.
		pm	Quiet but alert on ladder.
	3	am	Quiet but alert, active when stimulated. Vomit in tray. Pelleted faeces.
		pm	Huddled against front of cage, quiet, alert when stimulated. Dark faeces.
	4	am	Quiet but alert to external stimuli, sitting huddled on ladder. Normal faeces.
		pm	Sitting on perch, minimal response to stimuli.
	5	am	Quiet, huddled against front of cage, alert when stimulated.
		pm	Quiet and huddled at front of cage, reluctant to move. Dark faeces.
	6	am	Quiet but alert.
		pm	Quiet but alert.
	7	am	Quiet but alert. Loose faeces.
		pm	Quiet but alert. Loose faeces.
	8	am	Quiet but alert to external stimuli, huddled across ladder. Pale loose/liquid faeces.
		pm	Quiet but alert when stimulated.
	9	am	Quiet but alert. Green discoloured loose/liquid faeces.
		pm	Alert, quiet and huddled. Loose faeces.
	10	am	Quiet, huddled at front of cage, alert when stimulated. Loose faeces.
		pm	Quiet and huddled on perch. Loose faeces.
	11	am	Quiet and huddled, reluctant to move. Loose/liquid faeces.
		pm	Quiet and huddled on perch. Liquid faeces.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A164m (cont)	12	am	Huddled at front of cage, alert when stimulated. Loose faeces
		pm	Quiet and huddled on ladder, alert but difficult to stimulate. Loose faeces
	13	am	Quiet, huddled, subdued, minimal response to stimulation. Loose faeces. Sacrificed for humane reasons.
A89m	1	am	Bright and alert, huddled or occasionally lying on/across perch, sits up if stimulated.
		pm	Quiet but alert.
	2	am	Alert, aggressive, gentle activity. Dark faeces.
		pm	Alert, quiet, resting on ladder. Normal faeces.
	3	am	Quiet but alert. Vomit in tray. Dark faeces.
		pm	Quiet and huddled, alert when stimulated. Later – vomit in tray.
	4	am	Alert and active. Dark loose faeces.
		pm	Alert and active, vocalising.
	5	am	Subdued, sitting on ladder
		pm	Alert, resting on ladder, active when approached. Normal faeces.
	6	am	Alert and active.
		pm	Quiet but alert..
	7	am	Alert and active. Swelling lower abdomen.
		pm	Alert and active.
	8	am	Alert and active when stimulated. Loose faeces.
		pm	Alert, sitting on ladder, occasionally lying down.
	9	am	Alert but subdued. Vomit in cage. Pale/liquid faeces.
		pm	Signs not prior to sacrifice – Quiet and huddled, head between legs, reluctant to move. Sacrificed for humane reasons.
Y129m	1	am	Quiet but alert, sitting on ladder.
		pm	Quiet but alert. Pelleted faeces.
	2	am	Alert, gentle activity. Normal faeces.
		pm	Alert, gentle activity.
	3	am	Alert, fairly active.
		pm	Alert and active, moving around cage.
	4	am	Alert and active.
		pm	Quiet and huddled.
	5	am	Alert, fairly active, sitting on ladder..
		pm	Alert and active. Scrotum and prepuce appear swollen, red stained liquid on penis.
	6	am	Alert and active.
		pm	Alert, some activity.
	7	am	Alert and active. Dark loose faeces.
		pm	Alert and active.
	8	am	Quiet but alert, perched on ladder Loose faeces.
		pm	Alert, lying on ladder. Loose faeces.
	9	am	Alert, fairly active. Loose faeces.
		pm	Alert and active, vocalising, aggressive.

APPENDIX 11

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
Y129m (cont)	10	am	Quiet but alert, sitting on perch, aggressive and vocal when stimulated. Loose faeces.
		pm	Quiet but alert, fluid around abdomen and scrotum.
	11	am	Quiet and huddled, but alert. Mucus on loose faeces.
		pm	Quiet but alert. Loose faeces.
	12	am	Alert, gentle activity. Loose faeces.
		pm	Quiet and huddled, alert.
	13	am	Quiet but alert and active when stimulated. Loose faeces.
		pm	Quiet but alert, slight activity.
	14	am	Quiet but alert, appears bright. Loose faeces.
		pm	Quiet but alert. Swelling around stomach. Normal faeces.
	15	am	Quiet but alert, reluctant to move. Swollen abdomen. Loose faeces.
		pm	Signs noted prior to sacrifice – quiet, huddled, minimal response to stimuli, reluctant to move. Sacrificed for humane reasons
A77m	1	am	Quiet but alert if stimulated, sitting on ladder.
		pm	Alert and fairly active, sitting on perch.
	2	am	Alert, some activity. Loose/liquid faeces.
		pm	Very subdued, eyes closed.
	3	am	Quiet but alert, lying on ladder, active when stimulated.
		pm	Quiet but alert, occasionally huddled. Normal faeces..
	4	am	Alert, some gentle activity. Vomit overnight.
		pm	Quiet but alert, lying on ladder.
	5	am	Alert, some gentle activity. Vomit overnight. Loose black faeces.
		pm	Quiet and huddled, sits on cage floor, limited response when touched.
	6	am	Quiet, huddled, reluctant to move, abdomen swollen. Dark liquid faeces. Sacrificed for humane reasons.

APPENDIX 9

Individual clinical signs

Explanatory notes

1. Only first and last observations of the working day are reported. Due to manipulations/investigations performed on animals during the day, the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1).

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A170f	1	am	Animal sitting on perch, alert and fairly active.
		pm	Quiet but alert, sitting on perch, bruise on left forearm and back of both legs.
	2	am	Quiet but alert, sitting on ladder, bruise on left forearm, no faeces.
		pm	Alert and aggressive.
	3	am	Alert, some activity, grooming, no faeces.
		pm	Alert but quiet, sits on perch.
	4	am	Alert and active, moving around cage.
		pm	Alert, gentle activity, grooming.
	5	am	Moving around cage.
		pm	Quiet but alert, sitting on perch
	6	am	Appears bright and alert, occasionally active if stimulated but tends to sit on perch at front of cage.
		pm	Alert, occasionally active.
	7	am	Quiet but alert, sitting on perch, piloerection on shoulders, appears to be straining to pass urine.
		pm	Quiet but alert.
	8	am	Quiet but alert, active when stimulated, sitting at front of cage, loose faeces.
		pm	Alert and fairly active.
	9	am	Quiet but alert, sitting on ladder, moves when stimulated, piloerection, liquid faeces.
		pm	Alert, moving around when stimulated.
	10	am	Quiet but alert, loose faeces.
		pm	Alert and active.
	11	am	Quiet but alert, sitting on top of ladder, loose faeces.
		pm	Piloerection.
	12	am	Alert and active around cage, loose faeces.
		pm	Alert and active.
	13	am	Alert in cage, often moving around, sitting on top of ladder whilst resting head on hammock, loose faeces.
		pm	Alert on ladder, threatening.
	14	am	Quiet sitting on ladder, alert when stimulated, loose faeces.
		pm	Sitting quiet on hammock, grooming but is also alert.
	15	am	Alert but quiet in hammock, huddled.
		pm	Quiet but alert, piloerection, huddled, body tremors.
	16	am	Quiet but alert, sitting on ladder.
		pm	Quiet but alert if stimulated, sitting in hammock, body and limb tremors, dark loose faeces.
	17	am	Quiet but alert, loose faeces.
		pm	Quiet but alert, sitting in hammock.
	18	am	Bright and alert, active if stimulated.
		pm	Alert, some activity.
	19	am	Quiet but alert, sitting on ladder, loose faeces.
		pm	Alert, some activity, sitting quietly.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A170f (cont)	20	am	Alert, gentle activity if stimulated, loose faeces.
		pm	Quiet but alert, sitting in hammock.
	21	am	Quiet but alert, huddled, little movement, loose faeces.
		pm	Quiet but alert.
	22	am	Quiet but alert, no faeces.
		pm	Quiet but alert.
	23	am	Quiet but alert, huddled, loose faeces.
		pm	Quiet but alert, sitting in hammock, loose faeces.
	24	am	Alert, gentle activity, puffy under eyes, loose faeces.
		pm	Quiet but alert, sitting on perch, chewing ladder, no faeces.
	25	am	Alert, quiet and huddled on ladder, active when stimulated.
		pm	Alert and active.
	26	am	Alert and active.
		pm	Alert and active.
	27	am	Alert but quiet on ladder, gentle activity if stimulated, dark faeces.
		pm	Alert and gentle activity.
	28	am	Quiet but alert, sitting on ladder, moves slowly when stimulated but is unsteady.
		pm	Quiet but alert, piloerection.
	29	am	Quiet but alert.
		pm	Alert and active when stimulated.
	30	am	Quiet but alert, active when stimulated, liquid faeces.
		pm	Bright and alert when stimulated, sitting in hammock, no faeces.
	31	am	Quiet but alert, sitting on ladder, loose faeces.
		pm	Quiet but alert, sitting on hammock.
	32	am	Quiet but alert, loose faeces.
		pm	Quiet but alert, resting in hammock, loose faeces.
	33	am	Quiet but alert, loose faeces.
		pm	Alert but quiet, liquid faeces.
	34	am	Sitting on hammock, alert, moves when stimulated, liquid faeces.
		pm	Alert, some activity, grooming, loose/liquid faeces.
	35	am	Sitting in hammock, huddled, little movement, vocalising, liquid faeces.
		pm	Quiet but alert, sitting on ladder, no faeces.
	36	am	Sitting on perch alert, grooming.
		pm	Sitting on ladder, alert and active, loose faeces.
	37	am	Quiet but alert, sitting on ladder, grooming, moves slowly when stimulated, loose faeces.
		pm	Quiet but alert, loose faeces.
	38	am	Quiet but alert, sitting in hammock, moves slowly when stimulated, loose faeces.
		pm	Quiet, huddled, alert when stimulated.
	39	am	Quiet but alert, sitting on ladder, grooming, loose faeces.
		pm	Alert and fairly active.
	40	am	Alert, quiet, sitting on ladder, puffy under eyes, loose faeces.
		pm	Quiet and huddled.
	41	am	Quiet but alert, loose faeces, puffy around eyes.
		pm	Quiet but alert, loose faeces.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A170f (cont)	42	am	Quiet but alert, loose faeces.
		pm	Quiet, appears tired after dose.
	43	am	Quiet and huddled on ladder, alert to external stimulation, reluctant to move, loose/liquid faeces.
		pm	Alert, gentle activity, puffy under eyes, no faeces.
	44	am	Alert, sitting upright on ladder, loose/liquid faeces, swollen around eyes.
		pm	Alert, quiet in hammock, loose faeces.
	45	am	Quiet but alert, loose/ liquid faeces.
		pm	Alert, gentle activity, no faeces.
	46	am	Alert, active when stimulated, puffy around eyes.
		pm	Alert.
	47	am	Quiet but alert to external stimulation, sitting in hammock, loose faeces.
		pm	Alert, grooming, puffy around eyes, liquid faeces.
	48	am	Alert and bright, loose/liquid faeces.
		pm	Quiet, resting in hammock, puffy around eyes, loose faeces.
	49	am	Quiet but alert, sitting on perch, swelling around eyes, reluctant to move when stimulated, loose faeces.
		pm	Animal holding on to roof of cage, quiet and active, alert.
	50	am	Quiet but alert, sitting in hammock, loose faeces.
		pm	Alert, gentle activity, puffy around eyes, no faeces.
	51	am	Quiet but alert, loose faeces, active when stimulated.
		pm	Alert.
	52	am	Quiet and huddled, becomes alert when stimulated, moves slowly, swelling around eyes.
		pm	Alert and active, fluid build up around eyes.
	53	am	Quiet but alert, loose faeces, active when stimulated.
		pm	Alert, liquid faeces.
	54	am	Alert, sitting on ladder, loose/liquid faeces, puffy around eyes.
		pm	Quiet but alert, puffy around eyes and face, liquid faeces.
	55	am	Quiet but alert, puffy around eyes, active when stimulated, loose/liquid faeces.
		pm	Alert, occasionally huddled on ladder, eyes and face appear swollen.
	56	am	Loose/liquid faeces, quiet but alert, gentle movement when stimulated.
		pm	Puffy around eyes, alert, grooming, no faeces.
	57	am	Loose/liquid faeces, alert sitting in hammock, some movement, puffy around face and eyes.
		pm	Quiet but alert, eyes and face appear swollen, no faeces.
	58	am	Alert, puffy face especially around eyes, loose/liquid faeces, quiet and huddled on ladder, inactive.
		pm	Quiet and huddled, alert to stimulation, slow movements.
	59	am	Subdued and huddled, reluctant to move, piloerection, liquid faeces.
		pm	Asleep in hammock.
	60	am	Noted prior to sedation: lying on floor of cage, little movement even when stimulated, liquid faeces.
			Sedated and euthanased.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A166m	0		Animal died in surgery (donor kidney frozen during storage).
A176f	1	am	Quiet but alert, sitting at front of cage, blood staining on vet bed.
		pm	Sitting upright on perch and huddled but alert.
	2	am	Quiet and huddled, sitting on perch becomes alert when stimulated, unsteady when moving.
		pm	Alert and active.
	3	am	Alert and active.
		pm	Quiet but alert.
	4	am	Alert and active, climbing ladder.
		pm	Bright and alert moving around cage.
	5	am	Alert but looks tired sitting in hammock, quiet, no movement until stimulated.
		pm	Quiet but alert when stimulated.
	6	am	Quiet but alert, slow to react to stimuli, sitting on ladder.
		pm	Alert at front of cage.
	7	am	Alert and some activity.
		pm	Sitting in hammock, grooming and picking abdominal scar.
	8	am	Alert, active when observed.
		pm	Quiet but alert, sitting huddled, vocalising.
	9	am	Quiet, huddled in hammock, alert when stimulated, no faeces.
		pm	Bright and alert, grooming A167f through grid.
	10	am	Quiet but alert, loose faeces.
		pm	Alert and active.
	11	am	Quiet and huddled on perch but alert, loose faeces.
		pm	Alert, vocalising, liquid faeces.
	12	am	Quiet and huddled on ladder, alert when stimulated, loose faeces.
		pm	Alert, huddled.
	13	am	Alert and gentle activity, loose faeces.
		pm	Quiet but alert, sitting in hammock, dark faeces.
	14	am	Alert, huddled, loose faeces, no activity until stimulated, reluctant to move, loose faeces.
		pm	Asleep and quiet in cage.
	15	am	Alert and active.
		pm	Alert, moving around cage, abdomen distended, no faeces.
	16	am	Quiet and huddled on top of ladder, alert when observed.
		pm	Quiet but alert.
	17	am	Alert, gentle activity, loose faeces.
		pm	Quiet but alert, loose faeces, grooming, sitting on ladder.
	18	am	Alert, quiet, some activity when stimulated, loose faeces.
		pm	Alert and active.
	19	am	Quiet but alert, grooming perched on ladder, liquid faeces.
		pm	Quiet but alert.
	20	am	Alert, gentle activity, loose faeces.
		pm	Quiet resting in hammock, huddled, loose faeces.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A176f (cont)	21	am	Quiet but alert, sitting on ladder, body tremors, abdomen distended, bruising right side of abdomen, loose faeces, moves slowly when stimulated.
		pm	Quiet and huddled, alert when stimulated, abdomen appears distended, loose faeces.
	22	am	Huddled in hammock, loose faeces.
		pm	Alert, sitting on perch, grooming, active when stimulated.
	23	am	Alert, sitting in hammock, huddled, active when stimulated, no faeces.
		pm	Quiet but alert to stimulation, loose/liquid faeces.
	24	am	Quiet but alert, loose faeces.
		pm	Quiet but alert, body tremors, loose faeces.
	25	am	Alert, some activity around cage, loose faeces.
		pm	Alert, slow activity, loose faeces.
	26	am	Quiet but alert, sitting on cage floor, liquid faeces.
		pm	Alert but active, huddled.
	27	am	Animal sitting in hammock, huddled, reluctant to move, liquid faeces.
		pm	Quiet and huddled, alert.
	28	am	Alert, active around cage, vocalising, huddled, loose/liquid faeces.
		pm	Quiet but alert,.
	29	am	Alert and grooming.
		pm	Quiet but alert when stimulated, liquid faeces.
	30	am	Quiet and huddled in hammock, alert when stimulated, swelling around eyes, loose/liquid faeces.
		pm	Quiet but alert, sitting in hammock, huddled, loose faeces.
	31	am	Quiet but alert, swelling around eyes, loose faeces, huddled.
		pm	Alert and huddled in hammock.
	32	am	Alert and active, puffy around eyes, loose faeces.
		pm	Quite bright.
	33	am	Alert but quiet, huddled on ladder, puffy face especially around eyes, loose faeces.
		pm	Noted prior to sedation: prolonged periods of huddled, unsteadiness and reluctance to move. Sedated and euthanased.
A167f	1	am	Bright and alert, sitting on ladder, moves when stimulated.
		pm	Alert, sitting on top of ladder.
	2	am	Quiet but alert, standing on top of ladder.
		pm	Quiet but alert.
	3	am	Quiet but alert, grooming, active when stimulated, no faeces.
		pm	Bright and alert moving around cage, aggressive when approached.
	4	am	Alert, active, playing with toys, dark faeces.
		pm	Alert and active.
	5	am	Alert and active, dark faeces, vomit in cage.
		pm	Alert in cage.
	6	am	Alert and active.
		pm	Alert and threatening.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A167f	7	am	Alert, active, puffy around eyes.
		pm	Alert, some activity around cage.
	8	am	Alert, sitting in hammock, puffy around eyes.
		pm	Bright and alert, fairly active.
	9	am	Alert and active, moving around cage.
		pm	Bright and alert.
	10	am	Bright, alert and active.
		pm	Alert, huddled.
	11	am	Alert and active.
		pm	Alert, vocalising.
	12	am	Alert and active.
		pm	Alert and active, no faeces.
	13	am	Alert, grooming, loose faeces, active when stimulated.
		pm	Alert.
	14	am	Alert and active, loose faeces.
		pm	Quiet but alert, aggressive when approached, liquid faeces.
	15	am	Alert, sitting on top of ladder, dark liquid faeces.
		pm	Quiet but alert, loose/liquid faeces.
	16	am	Alert and active, puffy under eyes, loose faeces.
		pm	Alert and slow activity, loose faeces.
	17	am	Alert, quiet, huddled, loose/liquid faeces.
		pm	Quiet and huddled.
	18	am	Alert, perched on ladder, dark liquid faeces.
		pm	Quiet but alert.
	19	am	Quiet, resting on ladder, huddled, puffy under eyes, gentle activity when stimulated, liquid faeces.
		pm	Alert, quiet on ladder, puffy under eyes, liquid faeces.
	20	am	Quiet but alert, sitting on cage floor, swelling around eyes, bruising on right thigh, loose/liquid faeces.
		pm	Quiet and huddled, alert when stimulated but reluctant to move, swelling around eyes, abdomen appears distended, loose/liquid faeces.
	21	am	Quiet and huddled, vomit in tray, loose/liquid faeces.
		pm	Subdued, gentle activity.
	22	am	Quiet but alert, active when stimulated, liquid faeces.
		pm	Quiet and huddled but responding to stimuli, puffy around eyes, liquid faeces.
	23	am	Quiet but alert, sitting on ladder, loose/liquid faeces.
		pm	Quiet, huddled on ladder, alert when stimulated, loose faeces.
	24	am	Quiet but alert, sitting on ladder, loose faeces.
		pm	Alert, quiet, sitting on top of ladder, loose faeces.
	25	am	Quiet but alert, sitting on perch, loose faeces.
		pm	Alert and vocalising, huddled on ladder.
	26	am	Sitting on ladder, alert and fairly active.
		pm	Quiet but alert.
	27	am	Alert but quiet, huddled on perch, puffy around eyes, reluctant to move, liquid faeces.
		pm	Quiet but alert, lying in hammock, loose faeces.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A167f (cont)	28	am	Quiet, alert when stimulated, liquid faeces.
		pm	Quiet, huddled with partner.
	29	am	Quiet and huddled on perch, limb tremors, reluctant to move but unsteady when moving, appears to have difficulty using legs, swelling around eyes, abdomen appears swollen.
		pm	Quiet, huddled with partner, reluctant to move.
	30	am	Quiet and huddled, reluctant to move, swelling around eyes and abdomen, loose/liquid faeces.
		pm	Subdued, huddled with partner, black liquid faeces.
	31	am	Quiet and alert, huddled on perch, liquid faeces, puffy around eyes, reluctant to move but responsive to stimuli.
		pm	Noted prior to sedation: Very quiet, huddled oedematous swelling around eyes, reluctant to move, unsteady. Sedated and euthanased.
A174f			Noted prior to sedation: favouring use of upper limbs, flaccid paralysis of lower limbs, lower limbs cool to touch noted post operatively Day 0. Sedated and euthanased (shortly after midnight Day 0 to 1).
A457m	1	am	Quiet but alert, sitting on floor.
		pm	Quiet but alert if stimulated, occasionally active, no faeces.
	2	am	Quiet but alert, sitting on cage floor, small deposits of blood in tray, no faeces.
		pm	Alert, active if stimulated.
	3	am	Quiet but alert to stimuli, sitting on cage floor, picking at wound.
		pm	Alert but quiet, huddled on ladder.
	4	am	Quiet but alert, active when stimulated.
		pm	Alert and active, sitting on top of ladder.
	5	am	Alert and gentle activity, dark faeces.
		pm	Quiet and huddled, alert when stimulated.
	6	am	Alert but quiet, some movement.
		pm	Quiet in cage.
	7	am	Quiet but alert, active when stimulated.
		pm	Alert, moving around cage, normal faeces.
	8	am	Quiet but alert, some activity, loose faeces.
		pm	Alert.
	9	am	Alert and active, loose faeces.
		pm	Quiet but alert, loose faeces.
	10	am	Alert and active, loose faeces.
		pm	Alert and active.
	11	am	Alert and active, loose/liquid faeces.
		pm	Alert and active.
	12	am	Alert, gentle activity.
		pm	Quiet, resting in hammock, loose/liquid faeces.
	13	am	Quiet and huddled, sitting on ladder, alert when stimulated, some gentle activity, area around wound swollen, liquid faeces.
		pm	Quiet but alert, swollen scrotum, loose faeces, some gentle activity.
	14	am	Alert in cage, lip smacking at opposite monkeys, dark faeces.
		pm	Alert, active when stimulated.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A457m (cont)	15	am	Alert, lip smacking at other monkeys, active when stimulated, no faeces.
		pm	Quiet but alert to stimuli, area around eyes and wound swollen.
	16	am	Quiet but alert, sitting in hammock.
		pm	Alert and active, black faeces.
	17	am	Quiet, huddled on hammock, alert.
		pm	Quiet but alert.
	18	am	Quiet but alert.
		pm	Alert but quiet, huddled on hammock.
	19	am	Sitting on ladder, alert but not very active.
		pm	Alert and active around cage.
	20	am	Semi alert/sleeping.
		pm	Alert and active, small pelleted faeces.
	21	am	Quiet but alert, pelleted faeces, puffy around face.
		pm	Alert, active, puffy face, loose faeces.
	22	am	Quiet but alert, sitting on perch, face appears swollen especially around eyes, area around wound swollen, loose faeces.
		pm	Quiet but alert, face swollen, loose faeces, huddled in hammock.
	23	am	Quiet and huddled in hammock, face appears swollen, loose faeces.
		pm	Asleep in hammock.
	24	am	Quiet but alert, slight movement around cage, loose faeces.
		pm	Asleep in hammock.
	25	am	Alert, gentle activity, loose faeces.
		pm	Quiet on hammock.
	26	am	Quiet but alert, sitting in hammock, pelleted faeces.
		pm	Quiet and huddled, alert if stimulated.
	27	am	Quiet but alert, huddled in hammock, loose faeces.
		pm	Huddled in hammock.
	28	am	Quiet and huddled in hammock, puffy around eyes, eyelids partially closed.
		pm	Quiet and restful in hammock but alert, puffy face, area on abdomen swollen, loose faeces.
	29	am	Alert, eyelids partially closed, swollen abdomen, loose faeces, reluctant to move even when stimulated.
		pm	Noted prior to sedation: very distressed and having difficulty breathing, mucous membranes blue/grey in colour, animal collapsed. Sedated and euthanased.
A178f	1	am	Alert, bright but quiet, awake most of the night, red stained liquid/urine on vet bed.
		pm	Quiet, huddled over ladder, alert when stimulated.
	2	am	Alert, some blood in cage, little movement, huddled on perch, no faeces.
		pm	Alert in cage, appears to be straining.
	3	am	Sitting on perch, quiet but alert.
		pm	Quiet but alert, reluctant to move.
	4	am	Alert and active, no faeces.
		pm	Quiet but alert.
	5	am	Alert, friendly, gentle activity, dark faeces.
		pm	Alert, sitting at front of cage.
	6	am	Alert and friendly, gentle activity.
		pm	Quiet but alert.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A178f (cont)	7	am	Alert and active.
		pm	Quiet but alert.
	8	am	Alert, sits in hammock, gentle activity.
		pm	Alert, gentle activity.
	9	am	Quiet but alert, sitting on ladder, gentle activity when stimulated, bruising on right thigh.
		pm	Quiet but alert.
	10	am	Huddled, looks quiet in hammock, grooming.
		pm	Alert, active when stimulated.
	11	am	Alert, moving around cage, picking at wound.
		pm	Quiet but alert, no faeces.
	12	am	Quiet but alert, active when stimulated, loose/liquid faeces.
		pm	Alert, sitting in hammock.
	13	am	Quiet but alert, laying in hammock, loose faeces.
		pm	Quiet, resting in hammock, loose faeces, grooming.
	14	am	Quiet but alert, sometimes active, grooming, loose faeces.
		pm	Quiet, semi alert/sleeping.
	15	am	Thick liquid faeces, alert and active.
		pm	Quiet but alert, sitting in hammock, grooming, loose/liquid faeces.
	16	am	Semi alert in hammock, eyelids partially closed, liquid faeces, small amount of vomit, reluctant to move even when stimulated.
		pm	Quiet but alert, sitting in hammock, loose faeces.
	17	am	Quiet but alert, loose faeces.
		pm	Alert, loose faeces.
	18	am	Quiet but alert, sitting on ladder, moves when stimulated, liquid faeces.
		pm	Alert, liquid faeces.
	19	am	Quiet, occasionally huddled, liquid/loose faeces.
		pm	Alert, little movement when stimulated.
	20	am	Quiet but alert, sitting on ladder, loose faeces.
		pm	Alert and active.
	21	am	Alert, gentle activity.
		pm	Quiet and alert, huddled.
	22	am	Alert and active.
		pm	Alert and active, no faeces.
	23	am	Alert and active when stimulated.
		pm	Huddled in hammock.
	24	am	Quiet and huddled in hammock, reluctant to move even when stimulated, eyelids appear puffy, body and limb tremors, small pelleted faeces.
		pm	Alert, gentle activity, dark pelleted faeces.
	25	am	Alert, puffy around eyes, huddled posture in hammock, moves when stimulated.
		pm	Alert, quiet in hammock, no faeces.
	26	am	Alert and active, loose faeces.
		pm	Alert and quiet, loose faeces, puffy around eyes.
	27	am	Alert and very active, loose faeces.
		pm	Alert and fairly active.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A178f (cont)	28	am	Quiet and huddled on ladder, limb tremors when stimulated, face appears swollen especially around eyes, liquid faeces.
		pm	Alert, huddled, puffy around eyes, liquid faeces.
	29	am	Quite subdued, liquid faeces, puffy around eyes.
		pm	Alert but quiet and huddled, puffy around eyes, appears inactive.
	30	am	Huddled on perch, head raised only when stimulated, face swollen especially around eyes, eyelids nearly closed, unsteady on perch, does not move when stimulated.
		pm	Noted prior to sedation: Very quiet, unsteady, body tremors, grinding teeth. Sedated and euthanased.
A461m	1	am	Alert, some vocalising, no faeces, huddled.
		pm	Alert.
	2	am	Quiet but alert, sitting on cage floor.
		pm	Quiet but alert, some gentle activity when stimulated, pelleted faeces.
	3	am	Alert, sitting on ladder, pelleted faeces, food vomit.
		pm	Quiet but alert.
	4	am	Alert, gentle activity, dark pelleted faeces.
		pm	Quiet but alert, pelleted faeces.
	5	am	Alert, gentle activity, dark pelleted faeces.
		pm	Quiet but alert
	6	am	Quiet and huddled, perched on ladder, pelleted faeces.
		pm	Quiet but alert.
	7	am	Alert and active.
		pm	Alert, gentle activity, loose faeces.
	8	am	Quiet but alert, sitting on perch, moves slowly when stimulated, loose faeces.
		pm	Quiet but alert, scrotum swollen, loose/liquid faeces.
	9	am	Quiet in cage, sitting on perch, lip smacking, liquid faeces, fast to react when provoked.
		pm	Alert, active.
	10	am	Alert, sitting on top of ladder, picking at wound, liquid faeces, active when stimulated.
		pm	Bright and alert, loose/liquid faeces.
	11	am	Alert, sitting on perch, loose faeces.
		pm	Alert, sitting on cage floor, loose faeces.
	12	am	Quiet and alert, loose faeces.
		pm	Quiet but alert, loose faeces.
	13	am	Quiet but alert.
		pm	Alert and active, huddled.
	14	am	Alert and active, lip smacking, loose faeces, grooming.
		pm	Alert and active, loose faeces.
	15	am	Alert and active, lip smacking, vocal movement, loose/liquid faeces.
		pm	Alert and active, loose faeces.
	16	am	Alert and active, liquid faeces.
		pm	Alert and active, loose faeces.
	17	am	Alert and active, area around wound swollen.
		pm	Alert and active, liquid faeces.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A461m (cont)	18	am	Alert and active, area around wound swollen, liquid/loose faeces.
		pm	Alert and active.
	19	am	Alert and active, loose/liquid faeces.
		pm	Alert and active.
	20	am	Alert and active, loose faeces.
		pm	Quiet but alert.
	21	am	Quiet but alert, puffy around eyes, loose faeces.
		pm	Quiet but alert, loose faeces.
	22	am	Alert and gentle activity, loose faeces.
		pm	Quiet but alert.
	23	am	Bright , alert and active, soft faeces.
		pm	Alert, picking at sore on end of tail.
	24	am	Alert and active, loose faeces, vomit.
		pm	Alert and quiet on ladder, no faeces.
	25	am	Quiet but alert, loose faeces.
		pm	Alert, quiet and huddled, puffy around eyes, loose faeces.
	26	am	Alert, active, liquid faeces.
		pm	Alert, occasionally vocalising.
	27	am	Quiet and huddled but alert if stimulated, loose/liquid faeces, reluctant to move.
		pm	Eyelids partially closed, huddled on ladder, liquid faeces, no movement.
	28	am	Eyelids partially closed, huddled on ladder, licking sore on tail.
		pm	Alert, occasional gentle activity, huddled, slow movements, no faeces.
	29	am	Huddled on perch, raises head only when stimulated, very unsteady when stimulated to move, bruising on both forearms, thighs and scrotum appear swollen, dry scab-sore on tail.
		pm	Noted prior to sedation: below normal body temperature, collapsed posture. Sedated and euthanased.
A452f	1	am	Quiet, active when stimulated then returns to ladder and lays down, alert, no faeces.
		pm	Quiet and huddled, little response to stimuli, no faeces.
	2	am	Quiet but alert, lying in hammock, reluctant to move, some vomit.
		pm	Quiet but alert, huddled on ladder, loose dark faeces.
	3	am	Quiet but alert, sitting at back of cage becoming active when observed, loose faeces.
		pm	Quiet but alert, grooming, loose faeces.
	4	am	Quiet but alert, sitting on ladder, pelleted faeces.
		pm	Alert, vocalising, little activity, huddled.
	5	am	Sitting on ladder, grooming.
		pm	Quiet but alert.
	6	am	Sitting, alert but huddled, little movement, reluctant to move when stimulated.
		pm	Quiet but alert, aggressive when stimulated, pelleted faeces.
	7	am	Quiet but alert, huddled on ladder.
		pm	Quiet but alert, no faeces.
	8	am	Alert and active, moving around cage, loose faeces.
		pm	Quiet but alert, loose faeces.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A452f (cont)	9	am	Quiet but alert, loose faeces.
		pm	Huddled, reacts to stimulation.
	10	am	Quiet but alert, sitting in corner of cage, loose/liquid faeces.
		pm	Alert and active.
	11	am	Alert and active while observed, loose faeces.
		pm	Huddled on ladder.
	12	am	Quiet but alert, loose faeces, active when stimulated.
		pm	Quiet but alert, no faeces.
	13	am	Quiet but alert, loose faeces, grooming.
		pm	Alert when stimulated, sitting on hammock.
	14	am	Quiet and huddled but alert when stimulated, becomes aggressive, pale liquid faeces.
		pm	Alert but quiet and huddled on ladder, puffy around eyes, no faeces.
	15	am	Alert, vocalising, swollen face more so around left eye, no faeces.
		pm	Quiet, minimal activity.
	16	am	Alert, quiet, huddled, loose/liquid faeces.
		pm	Noted prior to sedation: alert but subdued, quiet and huddled, minimal activity. Sedated and euthanased.
A459m	1	am	Quiet but alert, small amount of blood in cage, no faeces.
		pm	Quiet, sitting in hammock.
	2	am	Quiet but alert, sitting on perch, appears to be straining to pass urine, reluctant to move even when stimulated.
		pm	Quiet but alert, loose/liquid faeces.
	3	am	Loose faeces, alert, occasional straining.
		pm	Sitting on ladder, alert, little movement.
	4	am	Quiet but alert, huddled on ladder, loose faeces, active when stimulated.
		pm	Sitting in hammock, huddled but alert, quite bright.
	5	am	Alert, gentle activity, loose faeces.
		pm	Huddled on ladder.
	6	am	Alert but quiet, loose faeces.
		pm	Alert, sitting on ladder, picking at wound.
	7	am	Quiet but alert, loose faeces.
		pm	Huddled in cage on ladder.
	8	am	Quiet and huddled but alert to stimuli, loose/liquid faeces.
		pm	Alert, sits on ladder, active if approached, no faeces.
	9	am	Alert, some activity around cage, vocalising, liquid faeces.
		pm	Alert, quiet on ladder, liquid faeces.
	10	am	Alert, gentle activity, loose faeces.
		pm	Alert, quiet on perch, dark liquid faeces.
	11	am	Alert, active, liquid faeces, open wound on abdomen.
		pm	Alert and fairly active, comfortable.
	12	am	Bright, alert, active, liquid faeces, open wound on abdomen.
		pm	Alert, picking at wet wound, some movement, liquid faeces.
	13	am	Alert and active, liquid faeces.
		pm	Alert, gentle activity, huddled, loose faeces.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A459m (cont)	14	am	Quiet but alert, active, wound open at base, bruise on right forearm, liquid faeces.
		pm	Grooming.
	15	am	Quiet but alert, sitting on ladder, loose faeces.
		pm	Alert, gentle activity, liquid faeces (noted when paired).
	16	am	Quiet but alert, grooming, loose faeces, active when stimulated.
		pm	Quiet, huddled on ladder, alert when stimulated, liquid faeces.
	17	am	Quiet and huddled, occasionally grinding teeth, alert when stimulated, reluctant to move, liquid faeces.
		pm	Alert, sitting on perch, vocalising.
	18	am	Alert, active, moves when stimulated, liquid faeces, vomit in cage.
		pm	Alert, watery faeces, light in colour, active when stimulated.
	19	am	Quiet but alert, liquid faeces.
		pm	Bright, alert, occasionally active, liquid faeces.
	20	am	Alert and active, loose/liquid faeces.
		pm	Alert, active, grooming, base of tail appears swollen.
	21	am	Quiet but alert, huddled on ladder, loose/liquid faeces.
		pm	Alert, movement around cage, no faeces.
	22	am	Loose/liquid faeces, vomit in tray, huddled in hammock.
		pm	Quiet but alert, sitting on ladder, no faeces.
	23	am	Alert, gentle activity, loose faeces.
		pm	Alert, active.
	24	am	Alert to stimuli, occasionally active, soft faeces.
		pm	Alert and active.
	25	am	Alert and active.
		pm	Quiet but alert, vocalising, loose faeces, active when stimulated.
	26	am	Alert, active while observed, loose faeces.
		pm	Alert and active.
	27	am	Alert and active, loose faeces.
		pm	Alert, gentle activity, liquid faeces.
	28	am	Quiet and huddled, responsive to stimulation, loose/liquid faeces.
		pm	Alert and active while observed.
	29	am	Quiet but alert, active when stimulated.
		pm	Alert.
	30	am	Alert, gentle activity, loose/liquid faeces, bright.
		pm	Alert, sitting on ladder, active when stimulated, huddled, black loose faeces.
	31	am	Alert and active, loose/liquid faeces.
		pm	Alert, gentle activity, no faeces.
	32	am	Alert, sitting in hammock, moves when stimulated, loose faeces.
		pm	Alert and active.
	33	am	Quiet but alert, active when stimulated, loose faeces.
		pm	Quiet but alert.
	34	am	Quiet but alert, loose faeces.
		pm	Quiet but alert, no faeces.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A459m (cont)	35	am	Quiet, huddled, alert when stimulated, loose faeces.
		pm	Quiet, huddled in hammock, alert when stimulated, liquid faeces.
	36	am	Appears bright and alert, occasionally active, scrotum and area around wound swollen.
		pm	Quiet but alert, liquid faeces.
	37	am	Alert, occasionally active, liquid faeces.
		pm	Huddled on hammock, lip smacking.
	38	am	Alert, occasional movement, liquid faeces.
		pm	Alert, active, vocalising, loose faeces.
	39	am	Alert but quiet, dark liquid faeces, puffy around eyes and face.
		pm	Quiet but alert, no faeces.
	40	am	Alert, subdued, liquid faeces, huddled, moves when stimulated.
		pm	Quiet, huddled, alert when stimulated.
	41	am	Quiet and huddled, liquid faeces.
		pm	Quiet but alert, sitting in hammock, liquid faeces.
	42	am	Alert, gentle activity and huddled, lower abdomen and scrotum swollen, liquid faeces.
		pm	Quiet and huddled on perch, loose faeces, breathing appears fast and shallow, reluctant to move even when stimulated, appears drowsy, face and area around wound swollen.
	43	am	Quiet but alert, loose faeces.
		pm	Noted prior to sedation: (observed following an episode of collapse) rapid breathing, very quiet and having difficulty balancing, not responding to stimuli.
			Sedated and euthanased.
A455m	1	am	Quiet and huddled, alert and responsive to simulation, no faeces.
		pm	Sitting on perch, huddled, alert when stimulated, grooming, abdomen appears distended, no faeces.
	2	am	Quiet and huddled, active and alert when stimulated.
		pm	Noted prior to sedation: very quiet and reluctant to move.
			Sedated and euthanased.
A464m	1	am	Quiet but alert, sitting on perch, active when stimulated, no faeces.
		pm	Alert, some gentle activity, sitting on perch, no faeces.
	2	am	Alert but reluctant to move, moves slowly when active, holding cage and ladder, appears a little weak.
		pm	Alert, restful, sits on cage floor, looks bright, not easily stimulated into activity, no faeces.
	3	am	Quiet, sitting on cage floor, appears alert, loose/liquid faeces.
		pm	Quiet and inactive resting on ladder reluctant to move, black loose faeces.
	4	am	Alert but eyelids partially closed, huddled on cage floor, reluctant to move even when stimulated then moves very slow and unsteady, dark green liquid faeces.
			Sedated and euthanased.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A469m	1	am	Alert, sits on perch looking around, some gentle activity.
		pm	Alert, sits on perch, looks bright but inactive, friendly, easily touched, black faeces.
	2	am	Quiet but alert, slow movements, pelleted faeces.
		pm	Quiet but alert, pelleted faeces, gentle activity.
	3	am	Alert, huddled, eyelids partially closed, dark semi loose faeces.
		pm	Alert, sitting on perch.
	4	am	Quiet but alert, occasionally active.
		pm	Alert and active.
	5	am	Quiet but alert.
		pm	Quiet but alert, no faeces.
	6	am	Quiet and huddled, alert when stimulated.
		pm	Alert when stimulated, quiet and huddled on perch, loose faeces.
	7	am	Alert and fairly active, area around wound swollen, loose/liquid faeces.
		pm	Quiet but alert, loose/liquid faeces.
	8	am	Quiet but alert, liquid faeces.
		pm	Quiet but alert, huddled.
	9	am	Alert, sitting on perch, general movement around cage, liquid faeces, swelling around stomach area.
		pm	Quiet but alert, responsive and active when stimulated, abdominal area swollen.
	10	am	Alert, active when stimulated, liquid faeces.
		pm	Quiet but alert.
	11	am	Alert, subdued, huddled on ladder, moves when stimulated.
		pm	Quiet but alert.
	12	am	Alert and active, liquid faeces.
		pm	Quiet but alert, sitting on perch, no faeces.
	13	am	Alert but huddled, reluctant to move, pale loose/liquid faeces.
		pm	Quiet and huddled on ladder, no faeces.
	14	am	Quiet but alert, loose faeces.
		pm	Quiet but alert, sitting on ladder, no faeces.
	15	am	Quiet but alert, red stained mucus around nostrils, loose faeces.
		pm	Quiet and huddled, no faeces.
	16	am	Alert, liquid faeces.
		pm	Quiet but alert, perched on ladder.
	17	am	Quiet and huddled at front of cage becomes alert when stimulated, reluctant to move, loose faeces.
		pm	Noted prior to sedation: subdued and huddled, eyelids closed, unsteady, not responding to stimulation. Sedated and euthanased.
A465m	1	am	Alert and occasionally active, sitting on perch, no faeces.
		pm	Quiet, perched on ladder, some movement.
	2	am	Quiet but alert, black liquid faeces.
		pm	Alert, active, sitting on ladder at front of cage.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A465m (cont)	3	am	Alert, sitting in hammock, vocalising, bruising around wound.
		pm	Quiet and huddled, alert and active when stimulated.
	4	am	Alert, active, sitting on ladder, moves when stimulated.
		pm	Alert.
	5	am	Alert, some activity, huddled, loose faeces.
		pm	Alert and active.
	6	am	Alert and active, liquid faeces.
		pm	Quiet but alert, active when stimulated, loose faeces.
	7	am	Alert, gentle activity, aggressive, threatening, dark loose faeces.
		pm	Quiet but alert, sitting on perch, grooming, no faeces.
	8	am	Quiet but alert, sitting in hammock, loose faeces.
		pm	Quiet and huddled, alert when stimulated, no faeces.
	9	am	Alert, active when stimulated, loose/liquid faeces.
		pm	Quiet but alert.
	10	am	Alert, active, sitting on ladder, liquid faeces.
		pm	Quiet, alert, grooming.
	11	am	Quiet but alert, grooming, liquid faeces.
		pm	Alert, restful in hammock, loose/liquid faeces.
	12	am	Alert, some gentle activity if stimulated, dark loose faeces.
		pm	Alert and active.
	13	am	Alert, quiet and huddled in hammock, swollen area from upper abdomen to thorax, loose faeces.
		pm	Quiet but alert.
	14	am	Alert but eyelids partially closed, huddled in hammock, little movement, liquid faeces, vomit
		pm	Quiet and huddled, alert when stimulated.
	15	am	Alert, gentle activity, aggressive, black loose faeces, huddled.
		pm	Quiet but alert, loose faeces.
	16	am	Quiet, dark loose faeces, responsive to stimuli.
		pm	Alert, active.
	17	am	Quiet but alert, vocalising, loose faeces.
		pm	Alert.
	18	am	Quiet, huddled, alert when stimulated, loose faeces.
		pm	Huddled but responsive.
	19	am	Quiet, huddled on hammock, loose/liquid faeces.
		pm	Wound opening and seeping, bandaged, active and alert, no faeces.
	20	am	Quiet and huddled on top of ladder, becomes active when stimulated, liquid faeces. Noted prior to sedation: subdued and huddled, body tremors, eyelids appear closed, no movement even when stimulated, no faeces. Sedated and euthanased.
A453m	1	am	Alert, bright, sits on ladder, gentle activity, no faeces.
		pm	Alert and active, blood in cage.
	2	am	Alert and active, sitting on ladder.
		pm	Alert, sitting in hammock.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A453m (cont)	3	am	Quiet but alert.
		pm	Quiet, alert.
	4	am	Quiet but alert, active when stimulated.
		pm	Alert, resting.
	5	am	Quiet but alert, appears to be straining to pass urine, swelling around wound.
		pm	Alert, gentle activity, bright.
	6	am	Alert, friendly, bright, gentle activity if stimulated, loose faeces.
		pm	Quiet but alert, responsive to stimuli.
	7	am	Noted prior to sedation: alert, quiet, some gentle activity, loose faeces. Sedated and euthanased.
A460f			Euthanased in theatre.
A456f	1	am	Alert, some gentle activity, holding top of cage, some stretching postures.
		pm	Quiet but alert, some movement around cage.
	2	am	Alert at front of cage, threatening, hard pelleted faeces.
		pm	Alert.
	3	am	Alert, clinging to front of cage.
		pm	Seems quiet but moving in cage.
	4	am	Alert, sitting on perch.
		pm	Looks good in cage, threatening and observant.
	5	am	Alert, sitting on perch, loose faeces.
		pm	Alert, huddled, no faeces.
	6	am	Quiet but alert sitting on ladder base, liquid faeces.
		pm	Alert, gentle activity.
	7	am	Liquid faeces, alert, moving around cage.
		pm	Alert and active, licking metal bars, no faeces.
	8	am	Quiet but alert, sitting on ladder, no faeces.
		pm	Quiet, sleeping on ladder, liquid faeces.
	9	am	Alert, sitting on top of ladder, grooming, liquid faeces.
		pm	Alert, responsive to stimuli, moving around cage.
	10	am	Alert but quiet, loose/liquid faeces, reluctant to move around much.
		pm	Quiet and huddled on perch, appears tired.
	11	am	Noted prior to sedation: animal alert when stimulated, otherwise quiet, brown loose faeces. Sedated and euthanased.
A463m	1	am	Alert, sitting on ladder.
		pm	Quiet sitting on ladder, no faeces.
	2	am	Alert when stimulated, no faeces.
		pm	Moving around cage, alert, responsive to stimuli, no faeces.
	3	am	Alert but quiet, dark faeces.
		pm	Alert on ladder, occasionally moving, occasional huddled.
	4	am	Alert but quiet, dark faeces.
		pm	Alert and active, moving around cage.
	5	am	Alert, some movement, generally active around cage.
		pm	Alert, some movement, vocalising.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A463m (cont)	6	am	Alert, gentle activity.
		pm	Subdued, alert when stimulated.
	7	am	Alert, gentle activity.
		pm	Alert.
	8	am	Alert, gentle activity.
		pm	Alert, moving around cage.
	9	am	Quiet but alert, sitting on cage floor, alert when stimulated.
		pm	Alert, grooming partner, vocalising, active.
	10	am	Alert, active.
		pm	Alert.
	11	am	Alert and active when stimulated, brown liquid faeces.
		pm	Quiet but alert, sitting on hammock, gentle activity, liquid faeces.
	12	am	Quiet and huddled in hammock, alert when stimulated, loose faeces.
		pm	Sitting on ladder vocalising.
	13	am	Quiet and huddled, alert when stimulated, loose faeces.
		pm	Alert.
	14	am	Alert and active, loose faeces.
		pm	Alert, active, liquid faeces.
	15	am	Quiet but alert, sitting in hammock, liquid faeces.
		pm	Quiet but alert, liquid faeces.
	16	am	Alert, gentle activity, dark liquid faeces.
		pm	Quiet but alert, sitting in hammock grooming, liquid faeces.
	17	am	Alert but quiet, some activity if stimulated, liquid faeces.
		pm	Alert and active.
	18	am	Alert and active, light brown liquid faeces.
		pm	Alert, active, vocalising, liquid faeces.
	19	am	Alert and active, liquid faeces.
		pm	Quiet but alert, loose faeces.
	20	am	Alert and active, liquid faeces.
		pm	Alert and active when stimulated, huddled, sitting on perch.
	21	am	Alert and active, moving around cage, liquid/loose faeces.
		pm	Alert, resting, some gentle activity, liquid faeces.
	22	am	Alert but quiet, gentle activity when stimulated, liquid faeces.
		pm	Alert, gentle activity, liquid faeces.
	23	am	Alert, liquid faeces, gentle.
		pm	Alert, liquid faeces.
	24	am	Alert, gentle activity, huddled, liquid faeces.
		pm	Alert and active, liquid faeces.
	25	am	Quiet but alert, slight movement on cage floor, loose faeces.
		pm	Quiet but alert, sitting in hammock, dry scabs on right shoulder, liquid faeces.
	26	am	Quiet but alert, sitting on ladder, active when stimulated, loose faeces.
		pm	Quiet, huddled, responsive when aroused.
	27	am	Quiet but alert, huddled on ladder, gentle movement when stimulated, liquid faeces.
		pm	Quiet and huddled on ladder, alert and gentle movement when stimulated, no faeces.
	28	am	Quiet but alert, sitting on ladder, loose faeces.
		pm	Quiet but alert, huddled, sitting on ladder, loose faeces.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A463m (cont)	29	am	Alert but quiet, gentle activity when stimulated, liquid faeces.
		pm	Quiet but alert, liquid faeces.
	30	am	Quiet but alert, sitting on perch, liquid faeces.
		pm	Alert and vocalising, active if stimulated, huddled on ladder, liquid faeces.
	31	am	Quiet, huddled in hammock, unresponsive to stimulation, reluctant to move, liquid faeces.
		pm	Alert and occasionally active.
	32	am	Quiet, alert when stimulated, huddled in hammock, liquid faeces.
		pm	Alert, sitting in hammock, liquid faeces.
	33	am	Quiet, sitting in hammock, appears swollen around eyes, alert, some movement when stimulated.
		pm	Alert.
	34	am	Alert and fairly active, liquid faeces.
		pm	Quiet and huddled in hammock, pale, liquid faeces.
	35	am	Noted prior to sedation: laying in hammock reluctant to move, shallow breathing, liquid faeces, puffy around eyes, subdued. Sedated and euthanased.
A451m	1	am	Quiet, lying on back on cage floor, no faeces.
		pm	Quiet, no faeces.
	2	am	Quiet, alert when stimulated, no faeces.
		pm	Alert, no faeces.
	3	am	Quiet but alert, food vomit, some activity if stimulated.
		pm	Active and alert, observant.
	4	am	Alert and active, moving around cage, black faeces.
		pm	Brown loose/liquid faeces.
	5	am	Alert and active around cage, grooming, vocalising, loose faeces.
		pm	Alert, sitting at front of cage, vocalising.
	6	am	Alert, gentle activity, fluid swelling around wound.
		pm	Alert, vocalising.
	7	am	Alert, friendly, gentle activity, dark faeces.
		pm	Quiet but alert, liquid faeces.
	8	am	Quiet, occasionally huddled, alert when stimulated, dark liquid faeces.
		pm	Huddled, alert, dark liquid faeces, gentle movement around cage.
	9	am	Quiet but alert, grooming, liquid faeces.
		pm	Alert, huddled on perch, some activity.
	10	am	Quiet but alert, dark liquid faeces.
		pm	Alert, dark liquid faeces.
	11	am	Quiet but alert, dark liquid faeces.
		pm	Quiet but alert, sitting on perch, active when stimulated, liquid faeces.
	12	am	Quiet but alert, huddled on perch, aggressive when stimulated, loose faeces.
		pm	Huddled on perch, resting.
	13	am	Quiet but alert, sitting on perch, loose faeces.
		pm	Quiet, occasionally huddled.

APPENDIX 9

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A451m (cont)	14	am	Quiet but alert, sitting on perch, loose faeces.
		pm	Some movement around cage, liquid faeces.
	15	am	Quiet and huddled on perch but becomes alert if stimulated, loose/liquid faeces.
		pm	Quiet and huddled, alert, liquid faeces.
	16	am	Alert but quiet and huddled, dark liquid faeces.
		pm	Quiet but alert, huddled on perch.
	17	am	Alert but quiet, occasionally huddled, active if stimulated, liquid faeces.
		pm	Alert, sitting on perch.
	18	am	Alert but quiet, occasionally huddled, active if stimulated.
		pm	Alert and active, vocalising, liquid faeces.
	19	am	Alert and active.
		pm	Quiet but alert,.
	20	am	Alert, sitting on perch, some movement around cage.
		pm	Sitting on perch.
	21	am	Alert but huddled, movement when stimulated, no faeces.
		pm	Alert but quiet and huddled, loose faeces.
	22	am	Alert but quiet, some gentle activity, loose/liquid faeces.
		pm	Alert, gentle activity, liquid faeces.
	23	am	Alert and active, grooming, liquid faeces.
		pm	Alert, liquid faeces.
	24	am	Alert, gentle activity, liquid faeces.
		pm	Alert but quiet and huddled, slight movement when stimulated, liquid faeces.
	25	am	Quiet but alert, sitting on perch, aggressive when stimulated, loose faeces.
		pm	Quiet but alert, loose faeces.
	26	am	Quiet but alert, sitting in hammock, aggressive when stimulated, loose faeces.
		pm	Sitting in hammock, alert and vocalising.
	27	am	Alert, sitting in hammock, liquid faeces, movement when stimulated.
		pm	Alert and active, dark loose faeces.
	28	am	Quiet but alert, active when stimulated, dark loose/soft faeces.
		pm	Quiet but alert, grooming whilst in hammock, black liquid faeces.
	29	am	Noted prior to sedation: alert but quiet in hammock, slightly puffy around eyes, reluctant to move when stimulated, liquid faeces. Passing urine very heavily contaminated with blood, hard swelling left side of suture line, very quiet, pained facial expression. Sedated and euthanased.
A462f	1	am	Alert, sitting up but minimal activity, lethargic, liquid bile like vomit.
		pm	Laying on stomach, scratching abdominal area.
	2	am	Lying down, reluctant to move, alert when stimulated, no faeces.
		pm	Sitting upright at front of cage on floor, alert but reluctant to move, no faeces.
	3	am	Noted prior to sedation: alert but subdued, vomited, very liquid faeces, very reluctant to move even when stimulated. Sedated and euthanased.

APPENDIX 10

Individual clinical signs

Explanatory notes

1. Only first and last observations of the working day are reported. Due to manipulations/investigations performed on animals during the day, the signs are considered to be unrepresentative of the underlying condition of each animal.

2. Clinical signs are reported from the day following transplant (Day 1).

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A171f	1	am	Alert. Sitting at front of cage. Occasional movement. No faeces. Slight straining.
		pm	Alert. Active if approached. No faeces.
	2	am	Alert but quiet. Active if stimulated. No faeces.
		pm	Unusual postures. Unsteady and slow when moving.
	3	am	Alert but quiet. Reluctant to move. Sitting on ladder. Black soft faeces.
		pm	Noted prior to sedation: Animal in state of collapse. No response to stimulation. No faeces. Sedated and euthanased
A172f	1	am	Alert, but eyelids heavy lidded. Sitting on perch. No faeces.
		pm	Alert and active. Moving around cage. No faeces.
	2	am	Alert but quiet. Active if stimulated. Sitting on perch. No faeces.
		pm	Bright and alert. Moves when stimulated. Sitting on perch. No faeces.
	3	am	Alert and active if stimulated. Gentle activity around cage. Normal/dark faeces.
		pm	Quiet but alert. Sitting on perch.
	4	am	Alert. Active when stimulated.
		pm	Alert. Scratching wound.
	5	am	Alert and active.
		pm	Sitting on ladder. Quiet and resting. Alert when stimulated.
	6	am	Quiet but alert. Huddled in hammock.
		pm	Alert, quietly grooming. Lying in hammock.
	7	am	Sitting in hammock, grooming leg. Appears alert.
		pm	Alert and active.
	8	am	Quiet but alert when stimulated. Sitting in hammock. Some red spots in tray.
		pm	Alert. Active when stimulated. Sitting on ladder. No faeces.
	9	am	Alert. Gentle activity.
		pm	Alert but quiet. Gentle movement around cage. Soft faeces.
	10	am	Alert. Sitting in hammock, grooming. Soft faeces.
		pm	Alert. Movement in cage. Appears slightly unsteady.
	11	am	Quiet but alert. Sitting on perch. Pelleted faeces.
		pm	Alert. Sitting in hammock. No faeces.
	12	am	Alert. Interested in surrounding environment.
		pm	Quiet but alert and responsive when approached.
	13	am	Alert. Gentle activity.
		pm	Alert and vocal. Active when stimulated.
	14	am	Quiet but alert to stimuli. Moves only in response to stimuli. Grooming/scratching wound on inner thigh of left leg.
		pm	Alert but quiet. Active when stimulated.
	15	am	Alert but quiet. Reluctant to move when stimulated.
		pm	Quiet, perched on ladder. Alert, occasionally grooming.
	16	am	Alert but quiet, resting left leg in hammock.
		pm	Quiet, lying in hammock. Alert to stimuli.
	17	am	Alert. Sitting in hammock. Little movement, even when stimulated.
		pm	Quiet, but alert. Resting in hammock. No faeces.
	18	am	Alert and active, moving around cage normally. No faeces.
		pm	Alert. Some activity around cage.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A172f (cont.)	19	am	Quiet but alert. Sitting on ladder.
		pm	Noted prior to sedation: Alert and active. Wound on leg opened fully. Sedated and euthanased.
A169f	1	am	Alert but huddled, lying on side on ladder. Small pellet of faeces. Gentle activity.
		pm	Quiet but alert. Sitting in hammock. Moves when stimulated.
	2	am	Alert and active around cage. No faeces.
		pm	Quiet but alert. Sitting in hammock.
	3	am	Alert and active. Diet vomit in hammock.
		pm	Alert. Sitting on ladder.
	4	am	Alert and active.
		pm	Alert and quiet. Lying on ladder, resting.
	5	am	Alert and active.
		pm	Alert. Quietly sitting in hammock.
	6	am	Alert and vocalising. Some movement.
		pm	Alert but quiet. Sitting in hammock. Dark liquid faeces.
	7	am	Quiet. Sitting in hammock. Alert when stimulated. Normal faeces.
		pm	Alert and active.
	8	am	Alert. Gentle activity. No faeces.
		pm	Alert and active if stimulated.
	9	am	Alert and active. Vocalising. Small pellets of faeces.
		pm	Alert. Vocalising. Appears steady in hammock. Active, grooming and foraging.
	10	am	Alert and active around cage.
		pm	Quiet but alert. Sitting in hammock.
	11	am	Alert and active in cage. Lot of movement and very responsive to stimulation.
		pm	Quiet whilst sitting in hammock. Eyelids open and alert. Active when approached.
	12	am	Alert and active.
		pm	Quiet and alert. Small pelleted faeces.
	13	am	Bright, alert and active.
		pm	Alert but quiet sitting in hammock. Soft faeces.
	14	am	Alert and active when stimulated. Eyelids partially closed. Sitting in hammock.
		pm	Alert. Active around cage, when approached becoming more aggressive.
	15	am	Alert and active. Vocal. Dark faeces.
		pm	Quiet but alert. Sitting in hammock.
	16	am	Alert and vocal. Some movement.
		pm	Alert and active.
	17	am	Alert. Sitting in hammock. Some movement when stimulated.
		pm	Animal died whilst undergoing biopsy.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A345f	1	am	Alert. Gentle activity.
		pm	Quiet but alert. Sitting on ladder. Moves when stimulated. No faeces.
	2	am	Alert and active. Some gentle activity around cage.
		pm	Alert. Sitting at front of cage on ladder.
	3	am	Alert and active around cage. No faeces.
		pm	Alert. Some activity.
	4	am	Alert. Lying in hammock. Movement around cage when stimulated.
		pm	Quiet and resting. Some movement.
	5	am	Alert. Grooming. Loose faeces.
		pm	Alert. Some movement around cage.
	6	am	Alert. Standing in cage and moving around. Dark pelleted faeces.
		pm	Quiet but alert. Grooming. Some vocalising. Dark faeces.
	7	am	Alert. Gentle activity. Fluid around wound. Loose faeces.
		pm	Alert. Sitting on perch. Active when stimulated.
	8	am	Alert. Brown, clear vomit. No faeces.
		pm	Quiet but alert. Sitting on ladder. Gentle movement when stimulated. No faeces.
	9	am	Alert and active. Some vocal activity. Normal faeces.
		pm	Quiet but alert. Responds to stimulation.
	10	am	Quiet but alert. Sitting on perch. Black pelleted faeces.
		pm	Quiet but alert. Sitting on ladder. No faeces.
	11	am	Alert and fairly active. Some quiet periods. Responsive when stimulated. Grooming.
		pm	Huddled on ladder. Alert when aroused.
	12	am	Alert and active.
		pm	Quiet and huddled. Alert when stimulated.
	13	am	Bright, alert and active. Fruit vomit in tray.
		pm	Alert, active when stimulated, but slightly quiet. Sitting on perch.
	14	am	Bright, alert and active.
		pm	Quiet, perched on ladder. Alert when approached.
	15	am	Alert and active.
		pm	Alert and active. Grooming.
	16	am	Alert. Lying on ladder, grooming.
		pm	Quiet and appears sleepy. Alert when stimulated. Sitting on perch. Huddled posture.
	17	am	Alert. Active when stimulated.
		pm	Alert. Sitting on ladder. Vocal.
	18	am	Quiet but alert. Gentle activity.
		pm	Quiet but alert. Straining to urinate.
	19	am	Alert and active. Occasional vocalisation. Soft faeces.
		pm	Alert and active when stimulated. Lying in hammock.
	20	am	Alert but quiet. Active when stimulated. Sitting on top of ladder.
		pm	Quiet but alert. No faeces.
	21	am	Alert. Sitting in hammock. Some activity.
		pm	Alert. Sitting in hammock. Aggressive when observed.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A345f	22	am	Alert and aggressive. Sitting on ladder. White frothy vomits on tray. No faeces.
(cont.)		pm	Quiet. Lying on ladder. Alert to stimulation.
	23	am	Alert and active. Aggressive. No faeces.
		pm	Alert. Grooming. No faeces.
	24	am	Alert and active. Loose faeces. Red staining noted on floor of cage.
		pm	Alert but quiet. Some movement. Huddled on ladder.
	25	am	Alert. Gentle activity. Loose/liquid faeces. Vomit.
		pm	Quiet but alert. Sitting in hammock. Gentle activity when stimulated. Loose faeces.
	26	am	Noted prior to sedation: Quiet and subdued. Reluctant to move. Loose/liquid faeces.
			Sedated and euthanased.
A472f	1	am	Sitting on perch, resting and quiet. Eyelids open and alert whilst being observed. No faeces.
		pm	Quiet. Huddled on perch at front of cage. Reluctant to move if stimulated, but opens eyelids and is alert to movement. No faeces.
	2	am	Quiet but alert.
		pm	Noted prior to sedation: Sitting on cage floor. Quiet and reluctant to move. No response to stimulation. No faeces.
			Sedated and euthanased.
A477m	1	am	Resting on cage front. Alert when approached. No faeces.
		pm	Quiet. Lying across ladder. Responds to stimulation. No faeces.
	2	am	Quiet. Alert when stimulated.
		pm	Quiet. Lying on perch. Eyelids closed. Some movement and alert when stimulated. No faeces.
	3	am	Noted prior to sedation: Quiet but alert.
			Sedated and euthanased.
A340f			Animal euthanased Day 0
A341m	1	am	Lying on cage floor. Sits up when stimulated. No faeces
		pm	Quiet but alert. Sitting on floor of cage. Gentle activity when stimulated. No faeces.
	2	am	Quiet. Sitting on floor at front of cage.
		pm	Animal removed from cage. Appears lethargic. Large amount of subcutaneous fluid noted.
			Sedated and euthanased.
A339m	1	am	Quiet. Sitting up. Eyelids partially closed.
		pm	Alert but quiet and reluctant to move. Sitting on cage floor. No faeces.
	2	am	Noted prior to sedation: Alert but quiet. Reluctant to move. Eyelids heavy lidded. Black faeces.
			Sedated and euthanased.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A467m	1	am	Quiet but alert. to stimuli. Occasional activity.
		pm	Alert. Active when stimulated. Sitting on perch.
	2	am	Alert but quiet. Gentle activity if stimulated. Some aggression.
		pm	Quiet but alert. Sitting on perch leaning on ladder
	3	am	Alert. Some gentle activity, aggressive No faeces. Deposit of clear mucus.
		pm	Quiet, resting on ladder. Alert to stimulation.
	4	am	Alert. Some movement.
		pm	Quiet but alert.
	5	am	Alert. Sitting on ladder. Active when stimulated. Quiet.
		pm	Alert but quiet.
	6	am	Quiet but alert. Area around wound swollen. Occasionally lying on ladder.
		pm	Alert and vocal. Some movement around cage.
	7	am	Quiet but alert, abdomen swollen.
		pm	Alert. Sitting on ladder.
	8	am	Quiet but alert, abdomen swollen.
		pm	Quiet but alert. No faeces.
	9	am	Alert, sitting on perch.
		pm	Alert. On ladder. Liquid/loose faeces.
	10	am	Quiet but alert, sitting on perch. Slightly active and aggressive when stimulated. Loose faeces.
		pm	Alert and active.
	11	am	Alert, some gentle activity. Soft/loose faeces.
		pm	Quiet but alert, sitting on ladder. Loose faeces.
	12	am	Alert. Active when stimulated. Loose faeces.
		pm	Quiet, huddled posture at back of cage. Little movement. Loose faeces.
	13	am	Alert, sitting on ladder, grooming. Active when stimulated. Loose faeces.
		pm	Quiet, huddled on perch, but alert. Active when stimulated. Loose faeces.
	14	am	Quiet but alert. Active if stimulated. Sitting on perch. Liquid faeces.
		pm	Sitting on perch, quiet but alert, huddled posture. Lifts head and looks around if stroked. Dark liquid faeces.
	15	am	Quiet, huddled on perch. Little movement even when stimulated. Loose faeces. Noted prior to sedation: Subdued and huddled on perch. Slight limb tremors. Does not respond to stimulation. Swelling seen around eyes and wound. Liquid faeces. Sedated and euthanased.
A476f	1	am	Alert but quiet. Reluctant to move.
		pm	Active around carge. Sitting on perch. No faeces.
	2	am	Alert and active.
		pm	Alert, perched on ladder.
	3	am	Alert. Not very active. Sitting on ladder. Some vocalising. Some pelleted faeces.
		pm	Alert, active when stimulated.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A476f (cont.)	4	am	Alert and active. Moving around cage. Soft faeces.
		pm	Alert, sitting grooming. Normal faeces.
	5	am	Quiet but alert.
		pm	Alert and vocal. Showing interest in outside surroundings and other animals.
	6	am	Quiet but alert.
		pm	Alert and observant. Slightly unsteady.
	7	am	Alert but quiet. Movement around cage when stimulated. Loose/normal faeces.
		pm	Quiet but alert. No faeces.
	8	am	Alert and active around cage. Loose/normal faeces.
		pm	Sitting on perch. Alert.
	9	am	Quiet but alert. Sitting on perch. Loose/soft faeces.
		pm	Alert, sitting on ladder. Normal faeces.
	10	am	Alert but quiet on perch. Some activity after stimulation. Loose faeces.
		pm	Quiet but alert when stimulated. Occasionally huddled on ladder. Liquid faeces.
	11	am	Quiet, huddled on perch. Some movement when stimulated. Loose faeces
		pm	Alert. Quiet and huddled. No movement.
	12	am	Alert and active. Loose faeces.
		pm	Alert. Picking at wound. Gentle movement when stimulated. Liquid faeces.
	13	am	Quiet and subdued. Reluctant to move. Picking wound. Liquid faeces.
		pm	Noted prior to sedation: Quiet and subdued. Huddled on perch, reluctant to move. Liquid faeces.
			Sedated and euthanased.
A338f	1	am	Alert. Crouching on cage floor. Reluctant to move when stroked. No faeces, no urine.
		pm	Noted prior to sedation: Quiet, reluctant to move, unresponsive to stimuli. No urine.
			Sedated and euthanased.
A475m	1	am	Alert, active and bright. Occasionally standing and bending over. No faeces.
		pm	Quiet but alert. Active if stimulated. No faeces.
	2	am	Quiet but alert, sitting at front of cage. Moves when stimulated.
		pm	Quiet but alert, sitting on ladder.
	3	am	Alert, gentle activity. Loose/soft faeces.
		pm	Alert, gentle activity. Swelling around abdomen.
	4	am	Alert, gentle activity. Loose faeces.
		pm	Quiet but alert. Sitting at front of cage.
	5	am	Quiet but alert. Perched on ladder.
		pm	Alert and vocal. Sitting.
	6	am	Alert and active when stimulated. Occasionally vocal.
		pm	Alert but quiet and huddled on ladder.
	7	am	Quiet but alert. Siting on ladder.
		pm	Alert and active. Vomit, food bile and liquid.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
A475m (cont.)	8	am	Alert, gentle activity.
		pm	Quiet but alert, lying on ladder. Occasional gentle movement.
	9	am	Lying on cage floor. Yellow discharge from nose.
		pm	Noted prior to sedation: Sitting on cage floor, resting against perch. Eyelids closed. Little reaction to stimulation. Clear nasal discharge. Sedated and euthanased.
A474f	1	am	Quiet but alert, siting at front of cage. Some gentle activity when stimulated. Piloerection.
		pm	Quiet, occasionally huddled, sitting at back of cage. Abdomen appears swollen. No faeces.
	2	am	Alert, quiet, occasional gentle activity. No urine, no faeces.
		pm	Noted prior to sedation: Subdued and huddled, sitting on floor of cage. Eyelids partially closed. Reluctant to move even when stimulated. Sedated and euthanased.
C101m	1	am	Quiet but alert. Pulling on bandage. Puffy around eyes
		pm	Quiet but alert. Gentle activity when stimulated.
	2	am	Alert, quiet, reluctant to move.
		pm	Alert and active. No faeces.
	3	am	Alert but quiet. Sitting on perch. Little movement even when stimulated. Straining to urinate. Noted prior to sedation: Quiet and huddled, no movement when stimulated. Sedated and euthanased.
C103m	1	am	Quiet but alert, gentle activity when stimulated. Face and around eyes appear puffy. No faeces.
		pm	Quiet but alert, sitting on ladder. Active when stimulated. No faeces.
	2	am	Alert but quiet. Swelling observed on lower abdomen. No faeces.
		pm	Quiet and huddled. Alert and gentle activity when stimulated. No faeces.
	3	am	Noted prior to sedation: Alert but quiet. Huddled on ladder. No movement when stimulated. No faeces. Sedated and euthanased.
C107m	1	am	Alert, gentle activity, aggressive. Dark faeces.
		pm	Alert, sitting on ladder. Active when stimulated. No faeces.
	2	am	Alert and active. Interested in outside surroundings. No faeces.
		pm	Alert and active. Good movement around cage. Liquid faeces.
	3	am	Alert and active, moving around cage. Loose faeces.
		pm	Alert, active at times. Slight bruising at base of wound. No faeces.
	4	am	Quiet but alert, active when stimulated. Slight bruising at base of wound and on right forearm. No faeces.
		pm	Alert and active.
	5	am	Alert and active.
		pm	Quiet but alert. Active when approached.
	6	am	Alert and active.
		pm	Alert and active.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
C107m (cont.)	7	am	Alert and active, moving around cage.
		pm	Alert, active, moving around cage.
	8	am	Alert, gentle activity.
		pm	Alert, gentle activity.
	9	am	Alert and active.
		pm	Alert, gentle activity. Sitting in hammock.
	10	am	Alert and active, normal movement around cage. Yellow mucous.
		pm	Quiet but alert, sitting in hammock.
	11	am	Alert and active.
		pm	Alert and active.
	12	am	Alert, active and vocal.
		pm	Alert and active.
	13	am	Alert, active and vocal.
		pm	Alert, gentle activity in hammock. No faeces
	14	am	Alert and active in hammock
		pm	Alert, gentle activity. Sitting in hammock.
	15	am	Alert and active. Soft faeces.
		pm	Alert, active when stimulated. No faeces.
	16	am	Alert, active and aggressive. Soft faeces.
		pm	Alert and active.
	17	am	Alert and active around cage.
		pm	Alert and active. No faeces.
	18	am	Alert, active when stimulated. Soft/Loose faeces
		pm	Alert and active moving around cage. No faeces
	19	am	Alert, active and aggressive. Soft/loose dark faeces.
		pm	Alert and active. No faeces.
	20	am	Alert and vocal. Some movement around cage. Dark faeces.
		pm	Alert in cage. Some salivation after dosing. Possible discomfort.
	21	am	Alert and vocal. Some movement around cage. Loose grey faeces.
		pm	Alert, vocal and active when stimulated. No faeces.
	22	am	Alert and active. Very active and agile when approached.
		pm	Alert, active when approached. Pelleted faeces.
	23	am	Alert and active. Active and aggressive when approached. Soft faeces.
		pm	Alert. Sitting quietly in hammock. Active if approached. No faeces.
	24	am	Alert and active.
		pm	Sitting in hammock, alert, lip-smacking.
	25	am	Alert and active when stimulated. Soft faeces.
		pm	Alert, gentle activity. Sits in hammock. No faeces.
	26	am	Alert and active.
		pm	Alert but quiet. Active when stimulated. No faeces.
	27	am	Alert, active when approached.
		pm	Quiet but alert, occasionally huddled in hammock. Liquid faeces.
	28	am	Alert and active when approached. Loose/liquid faeces.
		pm	Alert and active. No faeces.
	29	am	Alert and active. Loose faeces.
		pm	Alert but quiet, occasional vocalisation. Loose/liquid faeces.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
C107m (cont.)	30	am	Alert and active. Dark loose/liquid faeces.
		pm	Alert, sitting in hammock.
	31	am	Quiet but alert, sitting on ladder. Active and aggressive when stimulated. Liquid faeces.
		pm	Quiet but alert at rear of cage. Occasional movement. Abdomen swollen. Dark loose faeces.
	32	am	Quiet but alert. Sitting on ladder. Aggressive when stimulated. Loose/liquid faeces.
		pm	Quiet, huddled in hammock. Appears tired. Alert if approached.
	33	am	Alert and active when stimulated. Loose faeces.
		pm	Quiet, sitting in hammock. Alert, active and aggressive when stimulated. Liquid faeces.
	34	am	Alert and active when stimulated. Loose/liquid faeces.
		pm	Quiet but alert. Liquid faeces.
	35	am	Quiet but alert, sitting in hammock. Liquid faeces.
		pm	Noted prior to sedation:Alert and active, occasional vocalisation. Generalised piloerection. Liquid faeces. Sedated and euthanased.
C109m	1	am	Alert, quiet, occasional gentle activity. Dark faeces.
		pm	Alert, active when stimulated. Normal faeces.
	2	am	Alert but quiet, slightly huddled on ladder. Bruising around wound. No faeces.
		pm	Alert, gentle activity around cage when stimulated. Groom whilst siting on perch. Severe bruising round abdomen. Slight swelling around abdomen.
	3	am	Alert but quiet and reluctant to move. Severe bruising around abdomen. Slight swelling around abdomen.
		pm	Alert, sitting on ladder. Occasionally active, but slow moving. Grooming. Scrotum appears swollen. Severe bruising around abdomen.
	4	am	Quiet but alert. Moves when stimulated. Severe bruising around abdomen. Scrotum appears slightly swollen and bruised. No urine passed Sedated and euthanased.
C111m	1	am	Quiet. Occasionally siting on cage floor. No faeces.
		pm	Quiet, sitting on cage floor. Appears tired. No faeces.
	2	am	Quiet but alert, sitting on perch. Active when stimulated. No faeces.
		pm	Alert but sits quietly on ladder. Swelling of scrotum. Some swelling of both thighs. No faeces.
	3	am	Quiet but alert. Reluctant to move when stimulated. Sitting on cage floor. No faeces.
		pm	Quiet but alert, sitting on perch. Some swelling around base of wound. Scrotum swollen. No faeces.
	4	am	Quiet but alert. No faeces.
		pm	Quiet but alert, sitting on ladder. No faeces.
	5	am	Alert, but quiet. Some movement when stimulated. Sitting on cage floor. Straining to urinate. No faeces.
		pm	Quiet but alert to external stimuli.
	6	am	Quiet but alert, sitting on ladder. Active when stimulated.
		pm	Alert, gentle activity when stimulated. No faeces.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
C111m (cont.)	7	am	Alert but quiet. Sitting on cage floor.
		pm	Alert, sitting on perch. Gentle activity. No faeces.
	8	am	Alert, active. Soft faeces.
		pm	Alert and active. No faeces.
	9	am	Alert, active when stimulated. Straining to urinate. Green/normal faeces.
		pm	Alert and active.
	10	am	Alert but quiet. Reluctant to move when stimulated. Occasional vocalisation. Swelling around scrotum.
		pm	Quiet but alert, sitting on perch. No faeces.
	11	am	Alert, active when stimulated.
		pm	Alert, gentle activity.
	12	am	Sitting at front of perch. Little movement. Straining.
		pm	Quiet but alert.
	13	am	Alert and active. Some vocalising.
		pm	Alert. Some movement. Vocalising.
	14	am	Alert and bright, sitting on ladder.
		pm	Alert but quiet. Gentle activity when stimulated. No faeces.
	15	am	Alert and active. Scrotum swollen. No faeces.
		pm	Quiet and huddled on ladder. Alert and active when stimulated. Abdomen and scrotum appears slightly swollen. No faeces.
	16	am	Alert, active when stimulated. Abdomen and scrotum slightly swollen
		pm	Alert, sitting on ladder.
	17	am	Alert, active when stimulated. Scrotum and thighs swollen
		pm	Sitting huddled on ladder. Responsive when stimulated.
	18	am	Alert, quiet, active when stimulated. Scrotum swollen.
		pm	Alert, quiet, resting against ladder. No faeces.
	19	am	Alert and active.
		pm	Alert and active when stimulated. No faeces.
	20	am	Alert, active when stimulated.
		pm	Alert, gentle activity.
	21	am	Alert but quiet. Reluctant to move when stimulated. Huddled, sitting on ladder. Soft faeces.
		pm	Quiet but alert, occasional vocalisation. No faeces.
	22	am	Alert, occasionally sitting on ladder huddled. Scrotum appears swollen.
		pm	Alert and active, vocalising. No faeces.
	23	am	Alert but quiet, sitting on ladder. Reluctant to move. Light brown vomitus. No faeces.
		pm	Alert. Loose faeces.
	24	am	Quiet but alert, sitting on ladder. Active when stimulated. Loose black faeces.
		pm	Quiet and huddled on perch. Alert when stimulated. Scrotum appears swollen. No faeces.
	25	am	Alert, some activity when stimulated. Loose/liquid faeces.
		pm	Alert, some movement. Licking fingers.
	26	am	Alert, slow to move when stimulated. Slight puffiness under eyes. Loose/liquid faeces.
		pm	Alert but quiet. Tail appears swollen. Soft faeces.
	27	am	Alert, reluctant to move when stimulated. Loose/liquid faeces.
		pm	Quiet but alert, sitting on perch. Tail appears swollen. Dark liquid faeces.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
C111m (cont.)	28	am	Alert, sitting on perch. Loose/liquid faeces.
		pm	Alert, active.
	29	am	Alert, sitting on ladder, grooming. Liquid faeces.
		pm	Quiet but alert, sitting on ladder in huddled position. No faeces.
	30	am	Quiet but alert, sitting on perch. No faeces.
		pm	Alert, gentle activity. Liquid faeces.
	31	am	Alert but quiet. Little movement when stimulated. Slightly huddled posture. Liquid faeces.
		pm	Alert and vocal.
	32	am	Quiet but alert, sitting on perch. Slight piloerection around head and neck. Loose faeces.
		pm	Alert and vocal, sitting, slightly huddled posture. Little movement. Liquid faeces.
	33	am	Alert, some activity. Sitting on ladder. Soft/loose faeces.
		pm	Alert, gentle activity. Loose faeces.
	34	am	Alert, sitting on ladder. Active when stimulated. Soft faeces.
		pm	Unsteady on feet, but alert, vocalising. No faeces.
	35	am	Quiet but alert, sitting on ladder, huddled. Occasional vocalisation. Loose faeces.
		pm	Alert, active, occasional vocalising. Green/yellow liquid faeces.
	36	am	Alert but quite, sitting on ladder subdued. Loose/liquid green faeces. Tail very swollen. Sedated and euthanased.
C105m	1	am	Quiet but alert when stimulated. Lying on ladder. Dark faeces.
		pm	Quiet but alert, sitting on ladder. No faeces.
	2	am	Quiet but alert, sitting on ladder. Small pelleted faeces.
		pm	Alert, some gentle activity.
	3	am	Quiet but alert, gentle movement around cage. Brown/yellow vomit in tray. Pelleted faeces.
		pm	Quiet but alert, sitting on perch. Gentle activity when approached. Abdomen appears slightly swollen.
	4	am	Quiet but alert, aggressive and active when stimulated. Loose faeces.
		pm	Alert. Loose faeces.
	5	am	Alert, sitting on perch. Movement when stimulated. Loose faeces. Rectal mucus.
		pm	Alert and active. Loose faeces.
	6	am	Quiet but alert, sitting on perch. Loose/liquid faeces.
		pm	Alert, gentle activity. No faeces.
	7	am	Alert, gentle activity. Soft faeces.
		pm	Alert, gentle activity. Sitting on perch. Soft faeces.
	8	am	Alert, active. Soft faeces.
		pm	Alert, sitting on perch, grooming. Occasional movement. Loose faeces.
	9	am	Alert and active. Chewing ladder and toy. Soft faeces. Occasional salivation. Straining to urinate.
		pm	Sitting on perch. Very alert, active when stimulated. No faeces.
	10	am	Alert and active, normal movement.
		pm	Quiet but alert, sitting on perch.
	11	am	Alert and active. Straining to urinate.
		pm	Alert, gentle activity.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
C105m	12	am	Alert in cage, occasional activity. Occasionally sits huddled. Vomit in cage and tray.
(cont.)		pm	Quiet but alert. Liquid faeces.
	13	am	Alert and active. Some mucus discharge on mesh under cage. Liquid faeces. Some vomit.
		pm	Alert and vocalising.
	14	am	Alert and active. Moves when stimulated. Liquid faeces. Some vomit.
		pm	Alert and active. No faeces.
	15	am	Alert, gentle activity. Some vomit. Liquid faeces.
		pm	Alert, active when stimulated. Eyelids and scrotum swollen. Abdomen slightly swollen. No faeces
	16	am	Alert, active when stimulated. Eyelids slightly puffy. Abdomen and scrotum slightly swollen.
		pm	Alert, sitting on perch. Gentle activity if approached. No faeces.
	17	am	Alert, active when approached. Soft faeces. Food vomit. Scrotum, thighs and abdomen swollen. Large bruise on right arm.
		pm	Alert, sitting on ladder. Biting toe nails.
	18	am	Alert, active when stimulated. Sitting on ladder. Scrotum swollen. Slight swelling around eyes.
		pm	Alert, gentle activity. Scrotum and backs of thighs swollen.
	19	am	Alert and active. Scrotum swollen. Inner area of eyelids slightly swollen.
		pm	Alert, gentle activity when stimulated.
	20	am	Alert, active. Soft/loose faeces.
		pm	Alert. Bruising on legs and arms. No faeces.
	21	am	Alert, active when stimulated. Soft/liquid faeces.
		pm	Alert and active. Gentle movement when stimulated. Bruising on arms and legs. Back of thighs and scrotum swollen. Dark loose faeces.
	22	am	Quiet but alert. Puffy around eyes. Bruising on limbs, scrotum swollen. Loose faeces, brown vomit.
		pm	Alert, gentle activity when stimulated. Bruising and swelling on backs of thighs and scrotum. No faeces.
	23	am	Alert but quiet. Puffy around eyes. Backs of thighs and scrotum swollen and bruised. Dark and light loose/liquid faeces.
		pm	Alert, sitting on ladder. Backs of thighs and scrotum swollen. Loose faeces.
	24	am	Quiet but alert, sitting on ladder. Active when stimulated. Loose faeces. Vomit in tray.
		pm	Quiet but alert. Grooming. Swelling and bruising around scrotum and thighs. Swelling around both eyes. Dark loose faeces.
	25	am	Quiet but alert. Active and aggressive when stimulated. Loose faeces.
		pm	Alert, sitting on ladder, picking wound.
	26	am	Alert, active when stimulated. Puffy under eyes. Scrotum and thighs swollen and bruised. Soft faeces.
		pm	Alert, sitting on ladder. Active when stimulated. Puffy around eyes. Scrotum, thighs, lower legs and tail swollen. Soft faeces.
	27	am	Alert, active when stimulated. Thighs and scrotum swollen and light bruising. Dark loose faeces.
		pm	Alert, sitting on perch. Thighs swollen. Dark loose faeces.

APPENDIX 10

(Clinical signs - continued)

Animal no./sex	Day no.		Observation
C105m (cont.)	28	am	Alert and active. Thighs swollen. Loose faeces.
		pm	Alert and active. Moving around cage.
	29	am	Quiet but alert. Occasionally huddled on ladder. Thighs swollen. Loose faeces.
		pm	Quiet, eyelids partially closed. Alert when stimulated. Liquid faeces.
	30	am	Noted prior to sedation: Quiet but alert. Legs, abdomen, muzzle and arms swollen. Swollen around eyes. Sedated and euthanased.