REPORT BY CRUELTY FREE INTERNATIONAL AND SOKO TIERSCHUTZ

TOXICITY TESTING EXPERIMENTS ON NON-HUMAN PRIMATES, DOGS AND CATS AT THE LABORATORY OF PHARMACOLOGY AND TOXICOLOGY (LPT):

THE SUFFERING, THE CRUELTY AND THE POOR SCIENCE

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SECTION 1: INTRODUCTION

1. This report is the result of a joint investigation by Cruelty Free International (formerly the BUAV) (CFI), a UK-based animal protection organisation with international reach, and SOKO Tierschutz (SOKO-TS), a German animal protection organisation. The investigation took place during 2018 and 2019 at the Laboratory of Pharmacology and Toxicology (LPT), a contract-testing laboratory in Lower Saxony, Germany. An undercover investigator obtained employment at LPT as an animal keeper.

2. CFI campaigns against the use of animals in research. Its principal opposition to animal experiments is on ethical grounds but it also points to their often unreliable scientific value. For over 100 years, CFI has championed progressive, humane scientific research and cruelty free living. It runs an accreditation scheme in the EU for cosmetics and household products developed without animal testing.

3. While animal experiments continue, CFI seeks to ensure that they are properly regulated and, in particular, that (i) the harm:benefit test at the heart of EU member states’ legislation transposing EU Directive 2010/63 (the Directive)\(^1\) is applied in the rigorous way which the European legislators intended; (ii) suffering is kept to a minimum at all times, as the Directive requires; and (iii) alternative methods are used wherever possible, again as the Directive requires (this is known as ‘the Three Rs principle’: replacement, reduction [of numbers] and refinement). Refinement applies as much to the conditions in which animals are kept as to the experiments themselves. CFI has a strong track record of using the law to ensure that animals in laboratories receive the protection that they are meant to. For example, through the European coalition of animal protection organisations it leads it frequently takes part in appeals before the Board of Appeal of the European Chemicals Agency (ECHA), the principal EU regulator of industrial chemicals.

4. CFI strongly advocates an informed public debate on issues around animal experiments, which means that as much information as possible needs to be available to national and regional parliaments, the European Commission and the public. Given the secrecy which surrounds much animal experimentation, that includes the need for targeted undercover investigations. CFI has an unrivalled reputation for conducting such investigations around the world.

5. SOKO Tierschutz (SOKO-TS), based in Germany, is an advocate for animal rights as well as environmental and consumer protection. The organisation uses investigations - for which it, too, has an unrivalled reputation in Germany and neighbouring countries - to uncover the truth behind animal industries. The main focus is animals used in farming, research and the fur trade (including an investigation into raccoon dog farming in China). SOKO-TS has exposed numerous scandals in factory farming and, through media coverage, brought them

to national and international attention. This includes a recent investigation of an egg producer in Lower Saxony – under the same regulatory control as LPT.

6. SOKO-TS and its founder have also been involved in high-profile exposés of animal research in Germany. It believes that only an informed consumer and citizen can make ethical choices and only full and in-depth information can lead to an objective public debate about the use of animals for food, clothing and research.

7. **LPT** has three sites. The investigation took place at the Mienenbüttel site. The company provides toxicology services for the pharmaceutical (human & veterinary), industrial chemicals, agrochemicals, food and food additives and environmental (ecotoxicology) sectors. The company claims it works closely with regulators in the pharmaceutical and general chemical sectors such as BfArM (the German medicines regulator), the US Food and Drugs Administration (FDA), the European Medicines Agency (EMA), the European Chemicals Agency (ECHA) and the US Environmental Protection Agency (EPA). It has long conducted testing on batches of botulinum toxins (botox), a highly controversial type of testing causing very high suffering to tens of thousands of animals each year.

8. LPT uses the following species: monkeys (long-tailed macaques), dogs, cats, pigs, rabbits, mice, rats, hamsters, guinea pigs, fish and birds. However, the only reference to animal testing in the publicly-accessible part of its website is to ‘*in vivo* …toxicology’. The website says nothing about the type of animal tests it carries out, the species or the conditions in which animals are kept. On its website, the company describes its core values as ‘provid[ing] services of the highest integrity and excellent value, yielding strong and lasting client relationships, which are ingrained in our company culture’. It describes its work as ‘cutting edge’ and boasts of ‘high quality work’ and ‘scientific excellence’. The CFI-SOKO TS investigation shows that the reality is rather different.

9. The investigator’s areas of responsibility involved working with monkeys, cats, dogs and rabbits and included care of these animals, cleaning, assisting with examinations, determining body weights and food and drink consumption; clinical observations and checking equipment.

10. The investigator left voluntarily and was given a very positive reference.

11. The investigator took many hours of film. This included filming documents. They did not copy documents or remove them from the company. Inevitably, they were only involved in the care associated with a proportion of the animal testing work. They can only comment on what they came across and this report only deals with animal testing and care for which CFI and SOKO-TS have clear evidence.

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3 Taken from the reference given by the company when the investigator left
12. As with numerous previous investigations around the world, the investigation has revealed distressing suffering, wholly inadequate care of animals and systemic breaches of the law. Our findings are summarised in section 2 and set out in greater detail elsewhere. We have shown the footage to an experienced Emeritus Professor of Veterinary Medicine, Dr Nedim Buyukmihci, who has worked in an animal research laboratory. He is an expert in non-human primates, cats and dogs and he confirms our concerns. We refer to him as ‘CFI/SOKO-TS veterinarian’.

13. In this report we use the US National Academy of Science’s definitions of ‘stress’ and ‘distress’:

*Stress* responses are normal reactions to environmental or internal perturbations and can be considered adaptive in nature. *Distress* occurs when stress is severe, prolonged, or both….. Distress can follow both acute and chronic stress, provided that they body’s biological functions are sufficiently altered and its coping mechanisms overwhelmed* (our emphasis).

14. So poor is the culture of care and so high the suffering unnecessarily and routinely inflicted on animals that we believe that LPT should lose its authorisation to conduct experiments on animals. There should also be an inquiry, independent of the regulatory authority in Stade, Lower Saxony into the concerns we raise so that lessons can be learnt for the regulation of animal experiments more generally in Germany.

15. SOKO-TS has submitted a complaint to the state prosecutor.

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SECTION 2: SUMMARY OF KEY FINDINGS

Evidence of falsification of data

16. There is strong evidence that LPT acted fraudulently in one particular study involving non-human primates. From staff comments, it appears not to be an isolated incident. One monkey died, having been left with an untreated rectal prolapse. He was replaced on the study after some weeks by another macaque. The cage and study records continued to use the unique number of the original macaque during, as if it was the same individual.

17. Swapping the monkeys would distort the results of the tests, in several respects. We cannot be certain whether the customer, a South Korean company, gave its consent to the swapping of the macaques. It seems unlikely. If it did not, LPT deceived it. If it did give its consent, and the customer did not clear the swap with regulators of the drug used in the study around the world (which seems extremely unlikely), a fraud would have been perpetrated on those regulators and ultimately on patients.

Breaches of the law

18. We believe that LPT is systemically in breach of EU and German law. For example:

i. The cruel behaviour of some members of staff and the poor culture of care

ii. By allowing other forms of unnecessary suffering: In particular:

• Death should not be used as the ‘humane endpoint’ – the point at which the experiment should stop to avoid further suffering – save, exceptionally, for clear scientific reasons. One of the dog protocols – for a dose range-finding (DRF) study - did not specify a humane endpoint and the dogs were allowed to survive to the point where they were obviously extremely ill and suffering greatly. They were either allowed to die or be very close to death (moribund).

• The cruel and inappropriate use of the pole-collar method used to wrench macaques from their cages

• The restraint methods used on the macaques for transportation and procedures caused unnecessary suffering

• The way that the gavaging was carried out to administer substances to monkeys and dogs
• The way blood was taken from macaques, dogs and cats

• The fact that a macaque was left with a rectal prolapse for four days

• The lack of overnight care undoubtedly caused unnecessary suffering, given the nature of the tests and the adverse effects foreseen and experienced, including by the dogs

• The fact the macaques were forced to recover from general anaesthesia on metal bars

• The housing conditions: the paucity of environmental enrichment, the small cages, the single caging

• Allowing macaques, dogs and cats to witness procedures carried out on conspecifics, even euthanasia in the case of macaques

iii. Some of the housing breached the minimum standards set out in the directive

iv. The lack of adequate training given to staff

**Recommendations**

19. It is clear that immense suffering is caused to monkeys, cats, dogs and other animals at LPT. A high degree of suffering is inevitable, given the highly confined and unnatural conditions in which the animals are kept and the procedures to which they are subjected. However, there is also a great deal of avoidable suffering, in breach of the Directive and the TSchG.

20. The investigation has, once again, highlighted serious shortcomings in the regulation of animal experiments in Germany. It is clear that the European Commission shares at least some of these concerns.

21. The potential fraud relating to monkey 31M needs to be carefully investigated, but so do the innumerable breaches of animal protection legislation.

22. In our opinion, there is overwhelming evidence that LPT is not fit for purpose and should lose its authorisation to carry out animal experiments.
SECTION 3: EVIDENCE OF FALSIFICATION OF DATA

23. There are serious concerns that LPT falsified data from a study involving macaques and that staff regarded this as normal.

24. This related to a monkey known as 31M. He was one of 20 males on study 35497 (there were also 20 females). It was a 26-week study to assess the toxicity of a substance intended for use for endometriosis and uterine leiomyoma. The monkeys were given the substance daily for the 26-week period. Their health was monitored to assess the effects of the drug. Blood samples were taken, and the monkeys were killed and dissected.

25. The protocol reads:

‘Section 1.2 Duration of study:
Approximately 3 acclimatisation weeks
26 test weeks
16 recovery weeks for selected animals
Section 1.10 Study dates
Start of study (first dosing):
Main study and recovery animals: Females August 29th 2018, males August 30th 2018

Section 2.1 Number and sex of animals:
40 (20 male and 20 female) animals
In addition, 4 (2 male and 2 female) animals are available for possible replacement during the acclimatisation period.
Study termination
Main dissection: Females February 27th 2019, males February 28th 2019’

26. What follows is based in part on documents the investigator filmed and in part on conversations they had with several colleagues, including the head of the department.

27. The study started for the females on 29 August 2018 and on 30 August for the males. The study protocol anticipated that dissection would take place for the

5 Study 35497: A 26 week chronic toxicity study.
females on 27 February 2019 and for the males 28 February. Dosing followed a three-week acclimatisation period (a period for adjustment on arrival at the company). 31M died some weeks into the study (not during the acclimatisation period). This was as a result of a rectal prolapse. His intestines were found hanging out of his anus. A technician employed by LPT – who had never done the procedure before - tried to put them back in but was unsuccessful. According to staff, the monkey was left in that condition for four days before dying. That of itself raises extremely serious welfare concerns.

28. It is not clear whether 31M died as a result of the substance or for unrelated reasons. Intestinal prolapses are not uncommon in laboratory monkeys because of the stress which they endure; however, it could also be as a consequence of the substance.

29. There is overwhelming evidence that another monkey was then substituted. The study appears to have come to an end for the substitute monkey – also given the number 31M – at the same time as it would have ended for the ‘real’ 31M. The last date on which blood was taken from the substitute monkey was 28 February 2019 – the final day of the study.

30. Substitution of this sort would have serious implications for the integrity of the study, for three reasons. First, it would mean that the adverse effects experienced by the real 31M would not have been recorded. Second, the substitute monkey would not have been given the substance for the required 26 weeks. It seems highly unlikely that the study sponsor, a South Korean company, would have authorised the substitution but even if it did a fraud would have been committed on the relevant medicines regulators and ultimately on patients if the company presented the study results without drawing attention to the substitution. (It is possible but extremely unlikely that regulators around the world - in all the countries/regions where the sponsor intends to market the drug - would sanction the substitution). Third, the baseline and first few weeks of the study data were for a different individual, invalidating the results for one of the test animals in the study.

31. What is beyond dispute is that a substitute monkey was used. We know this because of the system of giving monkeys unique tattoo numbers (UTNs) on their chests. The real 31M’s UTN was 1601371 and that of the substitute monkey (clearly visible on his chest) was 1412447. 1601371 is the number on the cage for 31M and that remained there even after his death. The other monkey was put in that cage. 1412447 is not included in the UTNs for any of the 40 macaques officially in the study.

32. Even more damning, however, is the fact that, when the substitute monkey was killed at the end of the study, the tissue of the substitute monkey was labelled with the real 31M’s UTN. Clearly, there would have been no purpose in doing that had
he not been substituted. In addition, there is a sudden, significant change in the recorded weight of ‘31M’ around the time of the substitution.

33. Conversations between the investigator and (a) Person A, an experienced animal keeper, on 7 February 2019; (b) Person B, as she carried out an ECG on the substitute monkey on 27 February 2019; (c) Person C, another longstanding animal keeper, on 15 February 2019; and (d) the head of department, Person D on 4 March 2019 all confirm the substitution. Some of the staff indicated this was the practice at the company. Person C also explained in detail what happened with the rectal prolapse of the real 31M and the botched attempts to address it.

34. We acknowledge that we may not have the full picture on 31M, which makes it all the more important that the authorities investigate thoroughly.
SECTION 4: BREACHES OF ANIMAL PROTECTION LAW

35. There is clear evidence that LPT is guilty of systemic breaches of the law. These are not occasional examples of the company falling below the requisite standards: breaches are routine and inherent given the poor quality of staff, the general culture, the housing for the animals and the equipment and techniques used.

36. As explained above, it is a principle coursing through the Directive and the TSchG that suffering must be kept to a minimum at all times. That includes the conditions in which animals are housed, the care they are given, and the techniques used during the tests. It is important to stress that the unnecessary suffering to which the animals are routinely subjected is in addition to the suffering caused by the tests they are forced to undergo and the unnatural and confined conditions in which they are kept. That permissible suffering is itself often very high. To add unnecessarily to that suffering is not only unlawful; it is morally reprehensible. Some of the symptoms the animals could be expected to experience as a result of being forced to digest drugs and other substances are set out in the OECD guidelines referred to in paragraph 115 below.

A. Gratuitous cruelty and poor culture

37. It is obvious that gratuitous cruelty causes unnecessary suffering. It is also a breach of the TSchG.

38. During the investigation, there were several incidents of cruel and/or inappropriate behaviour by staff towards the monkeys in their care which the investigator recorded. Many of the incidents took place with the monkeys in Study 35497 when staff were catching and restraining the animals using the pole and collar method. These are examples, involving two members of staff, Person E and Person F.

Person E

39. In a conversation with the investigator, Person C said that Person E was no longer allowed with the dogs as a result of his treatment of them. It goes without saying that, if he could not be trusted with dogs, he could not be trusted with monkeys either and yet he continued to work with them.

40. Other incidents involving Person E which the investigator noted included:

- On 1 February 2019, he teased one monkey (1308040) with a broom stick by poking the animal through the bars of his cage.

- On 7 February 2019 (Study 35497), he tormented monkey (1110411) using vulgar language. Using the squeeze bar to force the monkey to the front of the
cage, he grabbed the animal’s tail and hind limbs and pulled them through the bars so that body was pushed hard against the cage bars. He also poked the animal through the bars to try to elicit a response. This continued for about 11 minutes.

- On 8 February 2019 (Study 35497), he hit a monkey on the head with a pole.

- On 11 February 2019, he threw a monkey back into the cage as though he was throwing a ball.

- On 12 February 2019 (Study 35497), he raised a pole to a monkey (as though he was going to hit the animal): the monkey was struggling as another member of staff was having difficulties locking the animal into the restraint apparatus.

- On 14 February 2019 (Study 35497), after pulling a reluctant monkey from his cage using the collar and pole method, he slammed the monkey’s head against the door frame as he took the animal from the room to be dosed in the corridor.

41. In a conversation with the investigator in February 2019, Person C commented that Person E liked to agitate the monkeys.

Person F

42. Recorded incidents involving Person F included one on 14 February 2019 (Study 35497) when he pulled a monkey out of the restraint apparatus following dosing. He swung the animal (who was attached by a collar to the pole) in the air and vigorously shook the pole. He then carried the animal back to the cage where he slammed him against the side of the metal cage before releasing the pole from the collar.

B. Lack of humane endpoints: dogs

43. Eight dogs were used in a DRF study for a Swiss company. Dogs were dosed daily via gavage starting on 25 January 2019 (the study was intended to run for 14 days). There were four dose groups, each containing 2 dogs (low, mid, mid-high and high dose). By the morning of 28 January (10am) three dogs (two in the high dose and one in the mid-high dose) were in a pitiful state, subdued, and passing blood.

44. Fresh blood appeared at times throughout the day. The rest pads were not in place in the cages, so during at least part of the day, the sick dogs were forced to sit or lie on the hard floor. By around 15:40-15:45 (near the end of the working day), the

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6 Study 36951: 14-Day Dose Range-Finding Study
three dogs were moribund; they had gone past the point at which they could survive. The definition of ‘moribund’ is ‘in the state of dying’ or ‘at the point of death’. In other words, they were non-responsive to their surroundings, including the investigator’s presence. They were dead by the next morning.

45. There is no doubt these dogs were allowed to deteriorate and left to suffer unnecessarily.

46. Another dog (from the mid-dose group) was also in a moribund state by the morning of 30 January 2019. The dog was found lying collapsed on their side, non-responsive with eyes open and blood on the ground.

47. The protocol for the study states:

‘3.1 Clinical signs
Every individual animal will be observed before and after dosing at each time of dosing for any signs of behavioural changes, reaction to treatment, or illness.

Kennel-side observations will include skin/fur, eyes, mucous membranes, respiratory and circulatory systems, somatomotor activity and behaviour patterns. The onset, intensity and duration of any signs observed will be recorded.

Daily records of the kennels will also be maintained (for vomit, blood, diarrhoea, etc).

Dated and signed records of appearance, change and disappearance of clinical signs will be maintained on clinical history sheets for individual animals.

In addition, animals will be checked regularly throughout the working day from 7.00am to 4.00pm. On Saturdays and Sundays animal will be checked regularly from 8.00am to 12.00 noon with a final check performed at approximately 4.00pm.

3.2 Mortality and moribundity
Further checks will be made early in the morning and again in the afternoon of each working day to look for dead or moribund animals. This will allow post mortem examination to be carried out during the working period of that day. On Saturdays and Sundays a similar procedure will be followed with a final check at approximately 4.00pm.

Premortal symptoms will be recorded in detail; as soon as possible after exitus, a post mortem examination as described in section 5.1 will be performed. In the case of prematurely scarified animals, blood sampling (see section 3.5 and 4) will be performed, if possible’.
48. Clearly, there is no point checking the dogs if nothing was then done to alleviate obvious and unnecessary suffering. Alleviation should include the killing of animals where this was called for. Video footage, taken during the day on 28 and 30 January 2019, depicting the appalling condition of the dogs, demonstrate that this was not done.

49. Furthermore, the protocol effectively sets the humane endpoint at death or moribundity. As is explained below, this is not necessary under European Medicine Agency (EMA) and Organisation for Economic Co-operation and Development (OECD) guidelines for repeated dose studies. Whilst there are no specific guidelines for DRF studies, the same principles should apply. The OECD guidance document 19 is an overarching document. There is no scientific justification for requiring death of the animals in a DRF and the Directive states that death as an endpoint should be avoided:

‘Article 13
Choice of methods
...
3. Death as the end-point of a procedure shall be avoided as far as possible and replaced by early and humane end-points. Where death as the end-point is unavoidable, the procedure shall be designed so as to:

(a) result in the deaths of as few animals as possible; and
(b) reduce the duration and intensity of suffering to the animal to the minimum possible and, as far as possible, ensure a painless death’ (emphasis added).

50. Article 24(2) then provides:

‘...
2. Member States shall ensure that persons specified in Article 40(2)(b) [the persons responsible for the overall implementation of the project and its compliance with the project authorisation] shall:

(a) ensure that any unnecessary pain, suffering, distress or lasting harm that is being inflicted on an animal in the course of a procedure is stopped; and

…’ (emphasis added).

51. Allowing the dogs in study 36951 to become moribund is a clear breach of these provisions, given that there was no scientific justification.
52. We are also concerned about the suffering and deaths of dogs in study 35733, a 4-week sub-chronic toxicity test. Between the 22 and 28 December 2018 at least 6 dogs from the mid-high and high dose groups were recorded as being dead.

53. These international guidelines outline that death is not required in regulatory toxicity studies and that animals should not be left in a moribund state:

   i. EMA Guideline on repeated dose toxicity (2010) ⁷

   ‘… a high dose, selected to enable identification of target organ toxicity or other non-specific toxicity, or until limited by volume of dose. Limit doses for acute, subchronic, and chronic toxicity studies of 1000 mg/kg/day for rodents and non-rodents are considered appropriate in all cases except those discussed in the Guideline ICH M3 (R2).

   ...

   Pain and distress in animals should be prevented or alleviated. Criteria for making the decision to kill animals who are experiencing severe pain or distress, and guidance on the recognition of predictable death, are the subject of OECD guidance document 19 (OECD, 2000).

   ii. OECD guidance document 19 ⁸

   ‘20. Guiding principles

   • ...
   • Severe pain, suffering, or death are to be avoided as endpoints
   • Studies must be designed to minimise any pain, distress or suffering experienced by the animals, consistent with the scientific objective of the study.
   • The earliest possible endpoints that are indicators of distress, severe pain, or impending death that should be used as indications for humanely killing the animals should be determined prior to the animals’ reaching a moribund state (12).

   Preliminary/Pilot Studies

   25. Preliminary or range-finding studies are often used to determine the appropriate dose-range to use in an experiment in the absence of other information about the test substance. The dose-range study should also be used to obtain data (using

clinical, biochemical, or other parameters) that can provide information useful to the identification of early endpoints as indicators of severe pain or distress which could be used in the decision to either complete the study, to terminate the study before the animals experience severe pain or suffering (12), or to determine whether analgesia or anaesthesia will be needed and can be used. If there is no information relevant to the determination of early endpoints as indicators of pain or distress, a separate pilot study may have to be performed. If a pilot study is performed, it should use only the minimum number of animals consistent with the objectives of the study. The information collected during range-finding or pilot studies should also be used to prepare or alert the study team for the actions or activities related to humane endpoints that may be needed.

43. Animals that are moribund or in a state of impending death should be humanely killed to avoid unnecessary pain or distress that they may be experiencing.

44. Impending death and/or moribund condition in laboratory animals can be indicated by various clinical signs and objective measurements (25)(26)(27)(28), some of which are shown in Table 1. Following adequate evaluation, a lesser degree of severity of these signs and measurements may also be useful indicators for predicting death, as previously defined. These signs and conditions typically include one or more of the following:
- prolonged, impaired ambulation preventing the animal from reaching food or water, or prolonged anorexia
- excessive weight loss and/or extreme emaciation and/or severe dehydration
- significant blood loss
- evidence to suggest irreversible organ failure
- prolonged absence of voluntary responses to external stimuli
- persistent, difficult laboured breathing
- prolonged inability to remain upright
- persistent convulsions
- self-mutilation
- prolonged diarrhoea
- significant and sustained decrease in body temperature
- substantial tumours
- other treatment-related effects judged to be indicative of impending death

54. OECD Test Guidelines do not require death as an endpoint. Animals humanely killed during the test will be regarded as dosage-dependent deaths' (emphasis added)
iii. **OECD Test Guideline 409 on 90 day repeated dose toxicity in non-rodents** states:

‘Unless limited by the physical-chemical nature or biological effects of the test substance, the highest dose level should be chosen with the aim to induce toxicity but not death or severe suffering’.

All this indicates that the purpose of a DRF prior to the conduct of a longer term repeated dose study such as the 90-day is not to identify the dose that would cause death but rather that would induce toxicity.

54. Best practice industry guidelines are to similar effect. According to the UK joint National Centre for the Three Rs (NC3Rs)/Laboratory Animal Science Association (LASA) report into DRF studies: 10

‘The clinical condition of an animal usually gives an initial indication that the test item is causing systemic toxicity. Due to the risk of unexpected or marked adverse clinical signs, the management of animal welfare issues is paramount in toxicology studies. This includes appropriate monitoring of clinical and other parameters and the use of humane endpoints.

The high dose for a regulatory toxicology study should produce signs of toxicity that are compatible with the study duration and are tolerated by the animal. This dose is referred to as the MTD (see Section 4.1) and is not expected to cause morbidity or mortality' (emphasis added).

55. The report goes on to say:

‘Table 2 contains examples of clinical signs of moderate severity adapted from this report for use in dogs. It is important to note that the descriptions in the moderate column in Tables 1 and 2 represent the upper limit of severity for identifying the MTD. Utmost importance should be given to determining humane endpoints, without reaching these levels of severity:

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56. It is clear from all this that dogs who were allowed to get into a moribund state suffered unnecessarily and that LPT is therefore in breach of both the Directive and the TschG. It also appears that, in practice, LPT unlawfully applied death as an endpoint without any scientific justification. The inescapable conclusion is that the company and its staff simply did not care about the suffering of the animals.

57. The CFI/SOKO-TS veterinarian comments:

‘The beagle dogs I saw were sometimes in a severely obtunded state (subdued, barely responsive to external stimuli, what we would term severely depressed in human patients). There is no question that these individuals were suffering greatly. In some cases, they had gone beyond this state and were moribund (collapsed, unresponsive to external stimuli, on the verge of death). Not only is it morally unconscionable to allow any individual to reach either of these states, there is no question that it was not necessary for the purposes of the study. That is, the study should have had as part of the protocol what is known as a 'humane endpoint'. This is standard practice in many laboratories and is required by many institutional animal use review committees. Such an endpoint takes into consideration the minimum effect on the animals to obtain the information needed and the potential for suffering on the part of the animals. In my professional opinion, this institution far exceeded any rational and practical humane endpoint and subjected these dogs to appalling and unnecessary suffering’.
C. Poor handling practices including lack of training (both of animals and staff), restraint, gavage and the taking of blood

58. There were numerous examples of poor handling practices, particularly of the monkeys, at LPT. The combined effect of poor techniques used to capture the monkeys, the attitude and behaviour of certain members of staff, poor apparatus used to restrain the animals and the lack of training and acclimatisation of the monkeys to handling and restraint would have caused additional, unnecessary suffering.

i. Lack of training of the animals for capture, handling and procedures

59. The monkeys should have been acclimatised (or ‘trained’) to the use of the collar and pole system, restraint apparatus and other procedures such as blood collection, as is recommended for welfare reasons. However, the behaviour of many of the monkeys shows that this was not carried out properly (if at all). Several animals became very distressed and agitated prior to and during capture, restraint and the carrying out of procedures.

60. For example, many of the monkeys in Study 35497, a 26-week chronic toxicity test involving daily oral administration of the test substance via oral gavage (see below), displayed extreme agitated behaviour, presumably in anticipation at what was about to happen to them. Anticipation of harm or danger results in further psychological stress, especially when the animals are subjected to a daily routine of potentially distressing procedures, such as the case with this study. Monkeys vocalised and displayed stereotypical behaviour, including circling, spinning and jumping inside the small confines of their cages. One male macaque from Study 35497 frantically circled backwards inside his cage.

61. Study 37001 was a DRF involving a single administration by intravenous infusion of eight monkeys followed by blood sampling (and other measurements) taken over the next 99 days. The protocol says the monkeys will be conditioned to the restraining chair during the week before dosing. The evidence is that this happened only once and did not involve positive reinforcement. The monkeys were merely put in the chairs for a short period of time.

62. Positive reinforcement involves the use of rewards such as food in return for cooperative behaviour. It does not involve the use of punishment. Acclimatising the monkeys to restraint- in the absence of positive rewards - cannot be considered appropriate ‘training’. Little (if any) positive reinforcement was used at LPT.
63. The training of non-human primates to cooperate in capture, handling and during procedures is considered good practice and is required under the Directive. Annex III in Section A: General section, states:

‘3.7. Handling

Establishments shall set up habituation and training programmes suitable for the animals, the procedures and length of the project’.

64. This is particularly important for non-human primates. An expert in the welfare of primates in the laboratory, Dr Sarah Wolfensohn, has said this:

‘Many experimental procedures require gaining access to the individual animal but since primates are intelligent they can be readily trained to cooperate even when they are living in social groups. Training is encouraged by the use of positive reinforcement, which may be in the form of a favourite food or drink which does not form part of their normal diet, they are not habituated to it...Training animals to cooperate with scientific, veterinary and husbandry procedures helps to reduce the stress that may be caused to both the animals and the laboratory staff’.

ii. Capture of animals: pole and collar method

65. The monkeys suffered considerable stress through the methods used to handle and restrain them. The callous and rough handling of the monkeys by certain staff also had the potential to cause injury. The noise of the cage doors and squeeze bars slamming along with staff shouting added to the overall stress.

66. The monkeys were fitted with a permanent rigid collar so that a pole could be fixed to it (pole and collar technique) and the animals removed from their cage. However, this was seldom achieved voluntarily, and coercion and physical force were used, resulting in considerable stress for the animals and putting considerable strain on the neck through the collar as well as the vertebrae from pulling on the tail.

67. The monkeys resisted attempts to have the pole attached to their collar and a struggle often ensued with the worker, resulting in the animal being forcibly dragged out of the cage. Sometimes, it took several attempts before the pole could be attached to the collar. Once out of the cage, the animals were swung towards the restraint apparatus where another struggle ensued as they resisted efforts to

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have the collar slotted and locked into place. This could take some time with the workers becoming agitated along with the monkeys. Methods used included holding the monkeys up in the air on the pole, shaking them and grabbing them by the tail. Workers were in a hurry and often rough with how they used the pole and squeeze bar.

68. Some workers became angry with monkeys resisting attempts to be captured from their cage (see above). Some staff were also rough in the way they returned primates to their cages following gavage. For example, on 11 February 2019, one member of staff (Person E) threw a monkey back into the cage as though he was throwing a ball.

69. Many of the monkeys became agitated, displaying behaviour consistent with extreme stress, repetitive circling inside their cages (one even circling in reverse around the small confines of his cage), struggling, screaming, cowering in the back of cage, refusing to leave.

70. In its report on the welfare of non-human primates used in scientific research, the European Commission’s Scientific Committee on Animal Health and Animal Welfare (EC SCAHAW)\(^\text{12}\) stated:

‘Primates are not domesticated animals and contact with humans can be extremely stressful, especially where the primates are not in control of the level and intensity of that contact, which is a particular problem in the laboratory’.

71. The least inhumane method of capture for macaques is to train them to enter a transport container.\(^\text{13}\) In its survey in 2017, the NC3Rs found that ‘approximately 2/3 of laboratories use an enclosed “box chair”, which the animal is trained to enter and then to extend its head through an opening on the top of the chair’.\(^\text{14}\) In 2009, the UK BVAAWF/FRAME/RSPCA/UFAW Joint Working Group on Refinement (the UK refinement group) discussed ways of handling non-human primates in laboratories. Referring to the use of the pole and collar method, it stated: \(^\text{15}\)

‘The working group considers that it is not good practice and does not recommend this method’.


\(^{13}\) Wolfensohn 2010. Ibid.


72. A review of capture practices in primate facilities in the UK by the UK Government’s Animals in Science Committee in 2013\textsuperscript{16} reported that:

‘Neck restraint was more commonly reported as having some adverse effects. The use of collar and pole (22 reports) was usual in only one establishment where it was reported as an alternative to the use of sedation (which was used in some other establishments) at the time of neck restraint. A collar and pole was used only to position the head in the chair and not to drag the monkey out of the cage. The use of these was for a very limited time only (days) and were deemed to be necessary and in the welfare interests of the animals to reduce the stress overall during this phase of training. No long-term adverse effects were reported. The use of collar and pole in the UK is rapidly declining’ (emphasis added).

73. It has long been established that it is possible to use only positive reinforcement (properly interpreted) with primates to facilitate a range of procedures including blood draws, handling for weighing and leaving the home cage. \textsuperscript{17} For example, the Porton Down Government primate facility in the UK has trained macaques to enter a transport cage from their home cage without using the pole and collar, using instead purely voice commands and grapes. The EU-PRIM (the European Primate Network which provides advice on the use of primates in research) has resources on positive reinforcement training. \textsuperscript{18}

74. Bliss-Moreau et al. \textsuperscript{19} reported much faster results using positive reinforcement to get macaques to enter a restraint chair and tolerate head restraint without the pole and collar (four weeks compared to a study by McMillan et al.\textsuperscript{20} which used the pole and collar and took 17 weeks). Their review shows that there are methods available that would cause less distress than those currently used by LPT - even supposing that staff showed compassion and empathy.


\textsuperscript{17} See various articles in Journal of Applied Animal Welfare Science, 6 93) 2003

\textsuperscript{18} http://www.euprim-net.eu/network/prt.htm# TrainingDVD


75. The CFI-SOKO veterinarian has commented on the pole and collar method used at LPT:

‘Given the extremely agitated and negative reaction to being secured with the pole and then removed from the cage, it seems that these monkeys have not been trained to the ‘pole and collar’ method of restraint and handling. Using this method without proper training defeats its purpose, which is to provide a humane and safe way to handle and move monkeys. These monkeys are, instead, being subjected to severe stress and the potential for significant injury. Not only is this inhumane, it unquestionably will have an uncontrolled impact on any information being derived from them’

76. The overall messages are clear: the pole and collar method does not have to be used; if it is, less suffering should be caused than was routinely the case at LPT.

iii. Restraint

77. Once removed from their cage, the monkeys were immobilised by their necks and forced to remain in a standing position for long periods of time in a restraint apparatus. Their fixed neck collars were slotted and locked into the apparatus which had wheels and was used to move the monkeys around the laboratory and to subject them to oral gavage and other procedures, such as blood collection and ECGs. This is not a normal position for macaques, having basically to stand on their hind legs and be unable to sit properly. It is something they would find extremely uncomfortable and stressful. If they tried to relax at all, then they would be only supported by their neck or they will have to hold onto the neck restraint device, so will always be in a state of stress and discomfort. Footage shows that they were clearly uncomfortable in this position and some displayed highly agitated and stressed behaviour – frantically turning their neck, rotating their bodies and spinning at a fast speed.

78. In study 37001, the monkeys were immobilised even more severely in another type of a restraint apparatus (a type of primate chair) in preparation for and during the infusion procedure, for a total of at least two hours. They were not well acclimatised to this procedure (see above) and clearly found it highly stressful.

79. On 20 February 2019, eight monkeys in this test were subjected to a 30-minute intravenous infusion into the vena cephalica. The animals were restrained by their necks and immobilised by having their front limbs strapped with sticky tape and their hind legs tied and taped together. In these apparatuses, the monkeys were placed in a row up against a wall facing the room. The process involved a member of staff taking the hind legs and front legs so that the monkey was 'hanging' by the neck until positioned - monkeys struggled and tried to twist their bodies. The monkeys' rear ends were supported by a platform, so the animals were in a sitting position. Their arms and hands were taped tightly with sticky tape to narrow
platforms protruding from the back of the restraint. A cardboard 'shield' was added between the tape and arms. The hind feet were also taped together tightly so that knees were in contact with each other (which can cause damage to the hip joints when prolonged like this). The result was that the monkeys were held rigidly and could only swivel their heads; with at least one monkey (number 1606043), the restraint around the neck was such that the head was pulled back into a 'chin up' position which would have created added discomfort. The monkeys were visibly traumatised by what was happening to them. Staff appeared oblivious to the impact their behaviour had on the monkeys; their loud voices, laughter and moving about vigorously while in the presence of these immobilised monkeys must have been frightening for the animals and added to their distress.

80. During the restraint, the monkeys had blood taken and their body temperature (via an anal probe) was then taken after the tape was removed. When the monkeys had their arms and legs freed from the tape, they would struggle to escape, often spinning by the neck. After having been strapped to the restraint apparatus for around two hours, the monkeys were returned to their single barren steel cages. The whole process can only be described as callous cruelty.

81. A number of researchers who use primates acknowledge that restraint causes stress and physical effects such that the animals seek ways to avoid it. 21 For example:

'It is important to recognise that restraint for any purpose and whether for short duration or longer may induce fear and stress responses such as physical resistance to handling, alarm vocalisations, defensive threatening and aggression, urination and defecation, and there will also likely be physiological responses that will increase unwanted data variability. 22 These fear and stress responses should be recognised as indicative of a serious welfare problem that must be properly addressed'. 23

82. The UK refinement group states that restraint chairs ‘can severely compromise animal welfare’ and ‘Any time longer than 1h, even for well-habituated animals, is likely to be a welfare concern’. 24


83. The EC SCAHAW report\textsuperscript{25} noted that:

‘There are … numerous reports which cite adverse electrophysiological, neuroendocrine or immunological sequelae as a consequence of such restraint… Moreover there are clear suggestions that habituation to the chair does not prevent the adverse biological impact of the procedure’.

84. A number of studies have demonstrated the negative psychological, physiological and physical reactions to restraint in primate chairs.\textsuperscript{26}

85. At LPT, there was little effort made to:

- train the monkeys to be as comfortable as possible in the chair (see above)
- use chairs designed to be comfortable to the individual monkey
- appreciate the stress of restraint and therefore reward the monkey during procedures

86. The CFI/SOKO-TS veterinarian comments on restraint:

‘Chairing monkeys is a serious animal welfare issue. Although I do not believe it is ever humane, steps can be taken to reduce the negative animal welfare aspects by carefully and compassionately training the monkeys to 'accept' the chair. The monkeys at this institution, however, clearly have not been trained and, as a result, resist vigorously to being chaired as evidenced by the violent spinning around and attempts to escape. Such physical exertions, particularly because the animals are restrained by the neck, can result in severe injury to soft tissues and neck vertebrae. There is also the issue of extreme restraint, which involved holding the head essentially immobile in space so that any relaxation of the monkey results in pressure on the neck. This is compounded by the monkeys not being supported in a way so as to mitigate the pressure on the neck’

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\textsuperscript{25} European Commission. 2002. Ibid.

iv. Blood withdrawal: monkeys

87. Blood collection took place either when monkeys were held in the restraint apparatus or while in their cages. Taking blood from a monkey while they remain in their cage is generally considered to be less stressful (though still stressful) than removing the animal into a restraint apparatus. Good practice requires ‘training’ (with the use of positive reinforcement such as food items) to encourage the animal to ‘present’ a limb to a member of staff. However, at LPT, this training appeared to be absent, and many monkeys became agitated and fearful and struggled as they were forced to the front of their cage by the squeeze bars (used to push a monkey to the front of a cage to facilitate removal from the cage or the taking of blood). One method used by some staff involved pulling the monkeys’ tail through the bars and using it to force the animal against the front of the cage while the hind limbs were dragged through the bottom bars of the cage. The tail and legs were then held together while the animal was pulled against the bars and blood taken from the rear of the hind limb. Pulling macaques around by their tails is bad practice as this species does not have prehensile tails and spinal injury could result. Many monkeys bled and had sores and bruising on their hind legs as a result. A bandage was applied to the sore, but the monkeys would invariably bite it off.

88. The UK refinement group\(^{27}\) says:

‘3.5.4 Training for procedures

It is possible to train primates to come to the front of a cage to present limbs for blood sampling or administration of substances to avoid the necessity of using a squeeze back (although with some pathogens, staff safety issues will be paramount). It may be easier to do this training before animals enter the containment facility, and time needs to be allowed for this’.

89. In addition, there are several reports of training macaques to present their arms or legs for blood draws. \(^{28}\)

90. The CFI/SOKO-TS veterinarian comments:

‘Many monkeys became agitated and fearful and struggled as they were forced to the front of their cage by the squeeze bars. Some staff pulled a monkey’s tail through the bars in order to force the animal against the front of the cage while the hind limbs were dragged through the bottom bars of the cage. The tail and legs were then held together

while the animal was pulled against the bars and blood taken from a hind limb. Because this species of monkey does not have prehensile tails, this type of handling could lead to spinal injury, particularly because of the violent struggling by the monkeys. The latter also caused unnecessary bleeding and soft tissue damage to the phlebotomy site. In contrast, monkeys can be ‘trained’ to offer their arm or leg for blood sampling while staying in their home cage. Not only is this more humane, it reduces the confounding variables introduced into the blood when derived from agitated and struggling animals’.

v. Blood withdrawal: cats

91. Each of the cats in study 36897 29 twice had 13 blood samples taken over a period of 10 hours following dosing of the test substance.

92. The cats were removed from their cages and physically restrained by one member of staff, who held the body with one hand and with the other pulled the cat’s head back, while another member of staff took the blood. Some of the cats became distressed and agitated when the blood was taken – they struggled and vocalised. The blood collection was carried out in view of other cats who could see and hear what was happening. Several cats had redness and/or bruising on their legs from the many needle insertions.

93. On 17 January 2019, one cat became very distressed having blood taken. The worker had a problem with inserting the needle into a vein. The cat’s leg already was sore. The cat vocalised and struggled whilst being restrained. The whole process took around 2 minutes and 20 seconds.

94. The lack of adequate socialisation of the cats made it more difficult for staff when handling the animals. Many staff were nervous about removing certain cats from their cages and restraining them for dosing or blood collection.

95. It is well-known that repeated blood sampling causes stress in animals used in experiments.30 If animals need to be repeatedly blood sampled, especially over short periods, then, to reduce their stress and to make blood collection easier, cannulation should be used. This is entirely feasible with cats. The UK NC3Rs 31 says this about the use of cannulae:

‘Cannulation is an important technique for removal of blood because it reduces the stress of multiple sampling associated with, for example, repeated restraint and needle sticks. Cannulation should be considered when repeated samples are required, especially over relatively short time periods’.

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29 Study 36897 Bioequivalence Study
31 https://www.nc3rs.org.uk/blood-sampling-or-general-principles#Cannulation
96. And, a European Federation of Pharmaceutical Industries and Associations (EFPIA)/European Centre for the Validation of Alternative Methods (ECVAM) report says: 32

‘Cannulation

This is an important technique for repeated bleeds. Temporary cannulae such as butterfly needles and over-the-needle cannulae can be used in the short term (working day), whereas for long-term use surgical implantation of biocompatible cannulae is required. These methods allow repeated blood sampling with minimal distress and discomfort for the animal’.

97. It is not clear why cannulation was not used in this study: there is no justification for not doing so in the study protocol.

vi. Gavage

98. Some of the studies involved monkeys being dosed via oral gavage. In study 35497, the monkeys were subjected to oral gavage daily for 26 weeks. This was highly stressful for them with cage banging by staff, loud metal on metal, staff often talking and shouting at each other almost continuously. The monkeys were removed from their cage (often with physical force) by the pole and their necks (with fixed collar) forced into the restraint apparatus. They were then pushed out into a corridor and forced into the uncomfortable apparatus described earlier. While one worker pinned the animal’s arms behind their back and clamped their hand over the mouth, another worker used a bite bar (with a pointed end) to prise open the animal’s mouth and force a rubber tube down their throat into the stomach. The contents of two syringes was rapidly injected through the tube.

99. The method used for oral gavage involved in Study 35497 poor practice and was potentially dangerous for the monkeys (there is no reason to think it was any different for other studies). The use of a pointed device to prise open the animals’ jaws was done with force and in a way that risked breaking teeth and causing other injury to the inside of the mouth. Some staff twisted the bar into the monkeys’ mouth with speed and without any apparent care that they might be causing pain or discomfort to the animals. Once the dosing had taken place, there was no checking to see whether there had been any harm caused to the inside of the animals’ mouth. Some monkeys suffered bleeding in their mouths following gavage. Regurgitation or vomiting also occurred followed the dosing.

100. No checks were carried out to ensure that the rubber tube was in the stomach and not in the lungs, of each monkey before the test substance was injected. The CFI/SOKO-TS veterinarian comments:

‘When using a stomach tube to introduce substances into an individual, proper medical procedure requires that the tube placement into the stomach be verified before attempting to inject the substance. Aspiration should be done using an empty syringe to feel if there is any resistance (lack of resistance suggests placement in the bronchus or lungs, resistance suggests, but does not prove, placement in stomach). The open end of the tube should be smelled to determine if the odour is consistent with gastric contents or is 'clear' suggesting air and, therefore, placement in the lungs. One should also place their face or eye close to the open end of the tube to determine if there are puffs of air coming out, which would be evidence that tube is in bronchus or lungs. Some people erroneously believe that a tube placed into the lungs will result in coughing or that coughing will occur as soon as material is injected, alerting the person to improper placement. There are several serious problems with reliance on this: 1) the individual may not cough; 2) a foreign substance, albeit a small amount if the technician is alert, will be injected into the lungs; and 3) the technicians at this institution injected the full amount of material rapidly, without any possibility of allowing a cough to alert them about incorrect placement. Not verifying placement is not only poor practice, it can lead to severe injury, illness and death from aspiration pneumonitis’

101. The UK refinement group has produced a report called Refining procedures for the administration of substances’. 33 With respect to gavage it said:

‘The technique

If the tube is incorrectly placed, if undue force is used, or if the animal moves, the tube may penetrate the trachea or pass through the oesophagus or stomach wall into the thoracic or peritoneal cavity. Subcutaneous abscesses may result from infection tracking out from the mediastinum, e.g. swellings in the axillary region. Repeated insertion of the tube for frequent dosing may cause inflammation and ulceration of the oesophagus. When a rigid gavage tube attached to a syringe is being used, negative pressure may draw in air, rather than create a vacuum, if the tube has inadvertently been inserted into the lungs rather than the oesophagus or stomach.

• Keep the animal still and ensure the best angle of the head and body to facilitate dosing. This is very important and requires correct and sensitive restraint. Be familiar with the anatomical relationships of the oropharynx and develop the necessary high degree of skill before commencing dosing to ensure accurate placement of the gavage tube.
• Always use the correct size (length and width) of feeding tube to ensure the dose enters the stomach and not the oesophagus. For example, in dogs the correct length corresponds to the distance from the nose via the acromion of the shoulder.

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to the tenth costochondral junction. Correct placement is confirmed by the smell of the gut contents. In mice the tube should extend from the tip of the nose to the last rib. Mark the length in advance.

- Make allowance for young or small individual animals.
- Check for condensation which may be visible if the tube has inadvertently been placed in the trachea.
- Use tubes with a small smooth knob on the end to prevent penetration of the gut wall. Flexible catheters are preferable to rigid tubes and plastic can be used instead of metal (but consider possible reactions between the compound and the tube). Consider lubricating tubes with petroleum jelly or medical paraffin to ease passage.
- If any resistance is felt during insertion of the needle, or if there is any sign of choking or distress, withdraw the tube and re-start the procedure. Always monitor the animal for a short period after returning it to its cage to check for any adverse reaction to the procedure and to check whether regurgitation or vomiting occurs. If animals die following oral dosing perform a necropsy examination to ascertain the cause of death and eliminate poor technique as a factor.
- If you suspect you have dosed into the lungs hold the animal’s chest close to your ear and listen for ‘gurgling’ or ‘rasping’ sounds. If the dose has gone into the lungs kill the animal to prevent further suffering.
- Gags can cause discomfort. Only use gags if they make the technique easier to perform and less stressful for the animal. Make sure any gags are designed to be comfortable for the animal. Tapering one end makes it easier to put into the mouth.
- The animal may regurgitate the dose or vomit. This is a particular problem with ferrets.
- Always expel the contents of the gavage tube at a controlled rate and withdraw the tube carefully. Monitor the animal carefully once it has been returned to the cage.

Primates

Oral gavage of Old World primates [such as macaques] should only be considered in cases where it is essential to ensure that the full dose of a drug reaches the stomach at the same time. It is a straightforward procedure provided staff are highly skilled and experienced in carrying it out. The stress of the technique is compounded by the stress of the restraint required and staff must be well trained and competent in this too. Lubrication of the tube will ease its passage. If at all possible, oral gavage should be avoided and substances should be administered orally by other means (emphasis added).

102. It is clear that the technique used at LPT fell far short of best practice and therefore added unnecessarily to the high degree of distress the monkeys were already experiencing. Technicians did not, as they should have done, routinely
check that substances had not been administered into the lungs. The restraint and use of the bite bar caused extra distress and injury.

103. It should be noted, finally, that, because of the stress that it causes, use of the gavage can affect the experimental results.  

vi. Post-anaesthesia care following fitting of neck collar

104. The monkeys were anaesthetised with Ursotamin (containing ketamine) which is an anaesthetic agent used during surgical procedures. They were injected in their cage (using squeeze bars to force them to the front) and then removed for the collar to be fixed on to their necks. They were then immediately returned to the cage and left to recover (regain consciousness), without adequate monitoring, on the bare bars of the cage floor. This is not good practice. They should have been protected with a soft surface so that they could not harm themselves when they started to recover (and throw themselves around the cage). A radio was blaring during this procedure: Ketamine is known to cause heightened sensitivity to ambient noise.

105. Several monkeys became extremely stressed and agitated prior to being anaesthetised for fitting of the neck collar. On 11 March 2019, three female monkeys (1507232, 1507548 and 1509398) became very agitated and displayed stressed behaviour, including spinning inside the cage.

D. Staff culture

106. With few exceptions, there was a lack of empathy from staff to the monkeys and an overall air of nonchalance, laughing and joking, often not looking at the monkeys while carrying out procedures. Such behaviour surely had to frighten and cause additional stress to the animals, especially as they were unable to flee. Staff did not treat the primates as highly intelligent sentient animals but more as objects, rarely taking notice of them as they wheeled them around the laboratory. The environment at LPT was noisy, compounding the stress.

107. One example: on 20 February 2019, during the intravenous infusion procedure for Study 37001, the investigator saw a worker shouting and throwing himself around leaning on the restraint apparatus in which the monkeys were immobilised with their arms and legs strapped. At least four staff members were present in this room making a lot of noise.

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108. In a conversation with the investigator in February 2019, Person C recalled how Person G, a laboratory technician, had asked her why she was so nice to ‘these dirty creatures’. Person C also commented on the futility, in her experience, of reporting malpractice within the company.

109. The general lack of empathy is particularly reprehensible given that staff were aware of the suffering regulatory toxicity testing causes animals. One member of staff, in a conversation with the investigator, noted the severe damage caused to the eyes of rabbits by dropping acetone into them, and also the futility of the test given the data available from workplace accidents.

E. Lack of overnight care

110. The hours of the animal staff were 7am to 4pm. According to study protocols, these were the hours when animals were supposed to be observed. One member of staff, Person H, an animal keeper, sometimes came in earlier than 7am for his own convenience. This was not a requirement of the company and was not to improve the quality of care for the animals. Even on those occasions, the animals would have been left unmonitored for at least 12 hours. There is no provision in protocols we have seen for out of hours care, even when clearly needed.

111. It is obvious, given the range and seriousness of the adverse effects which both were foreseen and happened in practice that this care regime was wholly inadequate to keep suffering to a minimum, as required by the Directive and TSchG. Animals are just as likely to suffer the foreseen adverse effects during the evening and night as during the day and there could just as easily be steps available then to reduce the suffering, or even where appropriate to end it by euthanasing an animal.

112. In any event, as noted above care was hopelessly inadequate even during the day.

F. Allowing animals to view procedures on, and the euthanasia of, conspecifics

113. LPT does not take adequate steps to minimise the stress to the monkeys by preventing or at least limiting their witnessing other monkeys being captured, restrained and subjected to dosing or procedures such as blood collection, or even euthanasia. The same is true of other animals.

114. On 15 March 2019, two monkeys were injected with barbiturate. They both immediately collapsed and were removed from their cages and placed directly into
a plastic bin with lid for dissection. This was carried out in view of other monkeys in cages in the room.

115. In Study 35497, monkeys were removed from their cages and restrained in the apparatus by their necks ready for oral gavage. Struggles with the pole were in the sight and hearing of the other animals in that room. The captured monkeys were either wheeled out (or carried out attached to the pole) into an adjoining corridor where the dosing took place. However, while one monkey was subjected to oral gavage, there was usually another monkey held in line in another restraint apparatus who could see and hear what was taking place.

116. The monkeys were also wheeled into the main area of the laboratory when other procedures were required such as blood collection and ECG. Here, the animals were lined up along a wall, in their restraint apparatus, facing the room and able to witness each other being transported and subjected to oral gavage and blood collection. Some animals displayed highly agitated and stressed behaviour – frantically turning their necks inside the restraint apparatus, rotating their bodies and spinning at a fast speed.

117. It is accepted that animals witnessing other procedures is a cause of unnecessary stress\textsuperscript{35}:

\textit{‘Several studies have addressed the possibility that merely witnessing other animals being subjected to procedures like those described above [blood collection, gavage, restraint] might be stressful’}

118. A number of studies have reached the same conclusion. For example:\textsuperscript{36}

\textit{‘… Macaques that were able to see other macaques being restrained and sedated for blood collection has higher cortisol levels than those that did not observe conspecific handling’}.\textsuperscript{37}

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\textsuperscript{35} Balcombe et al. 2004. Ibid.
\textsuperscript{37} Flow, BL and Jacques, JT. Effects of room arrangement and blood sample collection sequence on serum thyroid hormone and corticol concentrations in cynomolgus macaques (Macaca fascicularis). Contemp. Topics. Lab Anima Sci. 36, 6508. 1997.

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119. The UK Home Office\textsuperscript{38} recommends that animals are not allowed to see procedures on other animals.

‘It is advisable that regulated procedures, surgery or euthanasia are not performed in rooms where animals are normally housed or where other conscious animals are undergoing procedures, where this may cause additional avoidable stress to the animals. There should be separate preparation areas for animals, equipment and staff’.

120. The CFI/SOKO-TS veterinarian has commented:

‘… I think we can safely conclude that, at least in certain species (apes, macaques, rodents, birds, dogs), the observers can be aware of what is happening and react in ways that suggest they are stressed or they provide consolation to the one who was harmed when they are reunited. This can happen even if the observer only heard the other individual’s voice; they do not necessarily have to see what is being done. Therefore, when the researchers are doing noxious things (taking blood, giving injections and so forth), this should be done out of visual and auditory range of any other animal if one is concerned about the welfare of the animals.

H. Housing inadequacies

General legislative provisions

121. Annex III of the Directive provides:

‘Section A: General section

…

3.3 Housing and enrichment

(a) Housing

Animals, except those which are naturally solitary shall be socially housed in stable groups of compatible individuals. In cases where single housing is allowed in accordance with Article 33(3) the duration shall be limited to the minimum period necessary and visual. Auditory, olfactory and/or tactile contact shall be maintained….

(b) Enrichment

\textsuperscript{38} Home Office (December 2014) Code of Practice for the Housing and Care of Animals Bred, Supplied or Used for Scientific Purposes. P 68

All animals shall be provided with space of sufficient complexity to allow expression of a wide range of normal behaviour. They shall be given a degree of control and choice over their environment to reduce stress-induced behaviour. Establishments shall have appropriate enrichment techniques in place, to extend the range of activities available to the animals and increase their coping activities including physical exercise, foraging, manipulative and cognitive activities, as appropriate to the species. Environmental enrichment in animal enclosures shall be adapted to the species and individual needs to the animals concerned. The enrichment strategies in establishments shall be regularly reviewed and updated.

...

3.6 Resting and sleeping areas

a) Bedding material or sleeping structure adapted to the species shall always be provided, including nesting material or structures for breeding animals.

b) Within the animal enclosure, as appropriate to the species, a solid, comfortable resting area for all animals shall be provided. All sleeping areas shall be kept clean and dry' (emphasis added).

122. **Commission Recommendation of 18 June 2007** then adds guidelines: 39

‘4.5. Housing and enrichment

4.5.1. Introduction

All animals should be allowed adequate space to express a wide behavioural repertoire. Animals should be socially housed wherever possible and provided with an adequately complex environment within the animal enclosure to enable them to carry out a range of normal behaviours. Restricted environments can lead to behavioural and physiological abnormalities and affect the validity of scientific data….  

4.5.2. Housing

Animals, except those which are naturally solitary, should be socially housed in stable groups of compatible individuals. Single housing should only occur if there is justification on veterinary or welfare grounds…

4.5.3. Enrichment

All animals should be provided with sufficient space of adequate complexity to allow expression of a wide range of normal behaviour. They should be given a degree of control and choice over their environment to reduce stress-induced behaviour. This may be achieved by using appropriate enrichment techniques, which extend the range of activities available to the animal and increase their coping activities. In addition to

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social activities, enrichment can be achieved by allowing and promoting physical exercise, foraging, manipulative and cognitive activities, as appropriate to the species. It is advisable to allow the animals to exercise at every possible opportunity. Environmental enrichment in animal enclosures should be appropriate to the species-specific and individual needs of the animals concerned. Forms of enrichment should be adaptable so that innovation based on new understanding may be incorporated. The enrichment programme should be regularly reviewed and updated. The staff responsible for animal care should understand the natural behaviour and biology of the species, so that they can make sensible and informed choices on enrichment. They should be aware that all enrichment initiatives are not necessarily to the advantage of the animal and therefore should monitor their effects and adjust the programme as required (emphasis added).

Dogs

i. Single housing

123. In study 36951 40 (expected to last 14 days) the protocol (section 2.2, Housing and feeding) states that the dogs are kept singly, or in twos, if possible. Eight dogs were housed singly. There is no scientific or animal welfare justification given in the protocol for this.

124. Annex III to the Directive states:

‘Section B: Species-specific section
Section 4 Dogs
‘4. Dogs shall not be single-housed for more than 4 hours at a time’.

125. The Commission Recommendation states:

‘4.1 Single-housing of dogs for even short periods can be a significant stress factor. Therefore, dogs should not be single-housed for more than four hours without justification on welfare or veterinary grounds. Single-housing for more than four hours on experimental grounds should be determined in consultation with the animal technician and with the competent person charged with advisory duties in relation to the well-being of the animals.

In such circumstances, additional resources should be targeted to the welfare and care of these dogs. Additional human socialisation time, and visual, auditory and, where

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40 Study 36951 Dose range finding study.
possible, tactile contact with other dogs, should be provided for all single-housed animals on a daily basis.

Unless contra-indicated on scientific grounds, single-housed dogs should be allowed to exercise in a separate area with, if possible, other dogs, and with staff supervision and interaction, on a daily basis’ (emphasis added).

126. The UK Home Office says:\footnote{41}{Home Office Code of Practice p 99. Ibid.}

‘Single housing of dogs for even short periods can be a significant stress factor. Where they must be housed singly – on animal health or welfare grounds, or where permitted by Project Licence authority – additional human socialisation time, and visual, auditory and, where possible, tactile contact with other dogs is recommended on a daily basis’.

127. The UK refinement group\footnote{42}{Jennings, M. and Prescott, M.J. 2009. Ibid.} notes:

‘Toxicology studies have been carried out in the UK for many years now with pair housed or group-housed dogs, including good laboratory practice (GLP) studies, although it remains common practice to separate dogs for feeding and post-dose observations in such cases. Single housing in routine toxicology studies should therefore only be carried out when scientifically justified’.

128. It is clear from all this that dogs should not have been housed singly at LPT for the extended periods that some were. This caused unnecessary suffering.

ii. Enclosures

129. Beagles were housed in barren pens with a hard-tiled floor and with access to a small outside run attached to each pen.

130. All floors were hard with no shelves or substrate provided. Each pen contained one small pad which was made of a hard surface (polyethylene plastic), which had to be shared between two dogs (where dogs were in pairs), to provide relief from the floor. The pads should surely have been permanently on the ground, apart from cleaning and feeding periods. Dogs in at least two studies (36951 and 35733) who were bleeding as a result of the testing were sometimes not given resting pads during the day. Instead, they were forced to lie on the hard floor despite the severity of their suffering. During the day on 28 January 2019, very sick dogs from Study 36951 were filmed lying motionless on the hard floor of their cages. The rest
pads were not put down for them until later in the day— they remained attached to the side of the cage.

131. As noted, Annex III of the Directive says that bedding should be provided at all times and that it should be adapted to the species, solid and comfortable (see above).

132. The UK refinement group has produced a report entitled *Refining Dog Husbandry and Care*. It recommends that:

- All dogs should be provided with a warm, dry, draught-free area for resting and sleeping
- Facilities should consider providing beds and bedding for all dogs, both for comfort and environmental enrichment
- Beds are recommended for sick dogs, dogs in postoperative recovery and young pups.

133. Some of this clearly did not happen at LPT.

*iii. Enrichment*

134. As noted, Annex III of the Directive says:

‘Establishments shall have appropriate enrichment techniques in place, to extend the range of activities available to the animals and increase their coping activities including physical exercise, foraging, manipulative and cognitive activities, as appropriate to the species’.

135. The Commission Recommendation states:

‘4.2. Enrichment

The design of indoor and outdoor enclosures should allow some privacy for the dogs and enable them to exercise some control over their social interactions.

Separate areas for different activities should be provided. This can be achieved by, for example, inclusion of raised platforms and pen sub-divisions.

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https://www.nc3rs.org.uk/sites/default/files/pictures/Dogs/Prescott%20et%20al.%202004%20Refining%20dog%20husbandry%20and%20care.%20Laboratory%20Animals%2038%20S1%20.pdf
Dog treats and toys afford welfare benefits to the animals, providing these are used sensibly and adequately monitored. As chewing is an important behaviour, items should be provided which meet this need.

The primary advantages of exercise are to allow additional opportunities for dogs to experience a complex and varied environment and to increase interaction with other dogs and humans. These will be particularly important where these needs cannot be fully met within the space provided by the animal enclosure. Therefore, unless contraindicated on scientific or veterinary grounds, dogs should be removed to a separate area and allowed to exercise, with other dogs where possible, and with staff supervision and interaction, ideally on a daily basis’ (emphasis added)

136. The dogs had no platforms (raised areas) and were given no enrichment materials, i.e. toys, chews, etc.

137. The UK refinement group\(^{44}\) made these recommendations:

- Environmental enrichment is crucial in attaining high standards of welfare, and establishments should employ an appropriately qualified canine behaviour specialist to devise and develop an enrichment programme
- Enrichment items (e.g. chews, toys, plastic tunnels) should be provided in dog pens but these should not be seen as a substitute for social contacts, or to compensate for simple and boring accommodation
- Chewing is an important behaviour and items should be provided to meet this need. Chews that taste or smell of food (e.g. certain synthetic bones) will be more enriching
- Enrichment items should be presented in such a way as to maintain interest and activity (e.g. suspended off the floor and/or used on rotation)

138. There can be no doubt that housing for the dogs at LPT systematically fell far short of these standards.

Macaques

\(i.\) Single housing

139. The protocols stated for studies 37001\(^{45}\) and 36289\(^{46}\) that the monkeys would be housed individually: ‘The monkeys were housed individually in V2A steel cages with a size of 90cm x 82cm x 96cm’. That was indeed the reality.

\(^{44}\) Refining dog husbandry and care. Ibid.
\(^{45}\) Study 37001: Dose-Range-Finding Study
\(^{46}\) Study 36289: 9 week sub-chronic toxicity study
140. Study 37001 was a DRF study involving a single administration by intravenous infusion to eight monkeys followed by blood sampling (and other measurements) taken over the next 99 days. Study 36289 was a 9-week toxicity study involving 18 monkeys who received intravenous infusions of the test substance once every three weeks. The entire study actually ran for 64 days. The protocol made the same statement about housing as study 37001.

141. There is no justification given in either of the protocols for the single housing and it is difficult to discern what it could be.

142. Under Annex III of the Directive, macaques should only be housed singly in exceptional circumstances. 47

ii. Enclosures

143. The macaques were kept in two types of steel caging:

A. two tier, small, single steel cages with bars on the floor: the cages were barren with no shelf or resting area off the bars for the monkeys to retreat to. The lower cages were at ground level; the monkeys lived in semi-darkness. The walls between cages could be removed so, it was possible to have monkeys in pairs. However, the wall was opaque denying contact between animals when they were housed singly. Two rooms contained this type of caging and most monkeys housed in them were kept singly. Study plan 37001 and 36289 lists measurements for this type of cage as 90cm x 82cm x 96cm, a total volume of 0.71m3.

B. a set of three small single steel cages (with squeeze bars), each containing one monkey, which could be opened up within a small communal area enclosed with external steel bars to allow the monkeys to socialise. There were no shelves or structures in the single cages or the communal area. The monkeys were given access to the communal area to socialise between (12pm and 7am, i.e. afternoon and overnight). Some of these external steel bars had a small ‘balcony’ attached which allowed monkeys to look around the room, but not all.

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47 See Table 6.3 of section B of Annex III (footnote 14)
Table 6.3 (macaques and vervets) of Section B of Annex III of the Directive says:

<table>
<thead>
<tr>
<th>Animals less than 3 yrs of age (An enclosure of minimum dimensions may hold up to three animals)</th>
<th>Minimum enclosure size (m²)</th>
<th>Minimum enclosure volume (m³)</th>
<th>Minimum volume per animal (m³)</th>
<th>Minimum enclosure height (m)</th>
<th>Date referred to in Article 33(2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.0</td>
<td>3.6</td>
<td>1.0</td>
<td>1.8</td>
<td>1 January 2017</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Animals from 3 yrs of age (An enclosure of minimum dimensions may hold up to two animals)</th>
<th>Minimum enclosure size (m²)</th>
<th>Minimum enclosure volume (m³)</th>
<th>Minimum volume per animal (m³)</th>
<th>Minimum enclosure height (m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.0</td>
<td>3.6</td>
<td>1.8</td>
<td>1.8</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Animals held for breeding purposes (in breeding colonies no additional space/volume allowance is required for young animals up to 2 years of age housed with their mother)</th>
<th>Minimum enclosure size (m²)</th>
<th>Minimum enclosure volume (m³)</th>
<th>Minimum volume per animal (m³)</th>
<th>Minimum enclosure height (m)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.5</td>
<td>2.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For macaques and vervets, separation from the mother shall not take place before 8 months of age.

145. The Commission Recommendation⁴⁸ states in the general non-human primates section:

‘4.3.1. Dimensions

The following principles should apply to the housing of all species of non-human primates:

- enclosures should be of adequate height to allow the animal to flee vertically and sit on a perch or a shelf, without its tail contacting the floor,
- the animal should be able to display a normal locomotor and behavioural repertoire,
- there should be room for suitable environmental enrichment,
- apart from exceptional circumstances, the animal should not be singly housed,
- enclosures should not be arranged in two or more tiers vertically’ (emphasis added).

⁴⁸ Commission Recommendation of 18 June 2007. Ibid.
4.2. Enrichment

These animals, having advanced cognitive capabilities, require a suitably complex environment. A solid floor, which can be enriched by providing a non-toxic substrate, will allow for the concealment of scattered food items and encourage foraging. The enclosures should include vertical and diagonal structures for climbing, facilitating the use of the whole volume of the enclosure. Shelves and perches should not be placed one above the other. A space should be left between the shelf and enclosure wall to allow for the animal to suspend its tail freely.

Ladders, perches and toys to chew are all of value. In larger enclosures, a water tank (which is easily emptied) is particularly valuable for M. fascicularis but M. mulatta will also use it. Food can be dropped into the water for the long-tailed macaque and it will dive to retrieve it. Devices to encourage foraging (ranging from food scattered in the substrate to puzzle-feeders) have proved effective. Suitable food material can be placed on the mesh roof to encourage the animals to access it from the top of the enclosure. As novelty is important, toys should be provided and exchanged frequently.

4.3. Enclosures – dimensions and flooring

For the animals to feel secure, the design and interior dimensions of the enclosure should at least allow them to climb above human eye level (emphasis added).

147. In study 37001 (using A cages), the age of the monkeys was approximately three years; in study 36289 (also using A cages), they were between three and four years of age. The sizes of the two-tier cages (A) in these studies (0.71m$^3$ per monkey) were clearly below the EU requirements specifying a minimum volume of 1.8m$^3$ per animal. There was no justification in the study protocol for the cage sizes being below the minimum legal requirements. Nor could there be any.

148. Furthermore, the A cages fell short of the EU Recommendation by their nature of being two-tier. This additionally meant that monkeys in the lower tier could not flee above human eye level, another requirement of the EU Recommendation.

149. In neither type of cage systems (A or B), were there perches provided within the cage, save for the balconies in some of the B cages. Monkeys in study 35497 were in B cages that did not have these balconies. The EU Recommendation requires that perches are provided.

150. Once again, it is clear that LPT falls far short of the requisite standards and that the monkeys therefore suffered unnecessarily on a constant basis.
iii. Enrichment

151. The monkeys spent their entire lives in a barren environment. There was no effort to provide them with any regular and meaningful enrichment. There was the very occasional projection of a film on a television screen installed at the end of the monkey rooms (although there were not enough screens for each of the rooms). Also, on two occasions the investigator saw that a single bowl of water for the monkeys to play in was briefly provided. This was totally inadequate for a species that requires an enriched and stimulating environment in captivity.

152. Close confinement in barren surroundings with no enrichment would be highly stressful for these monkeys, especially those housed singly, and this is supported by the abnormal behaviour witnessed. Several of the monkeys at LPT exhibited stereotypical behaviour; including repetitive circling, jumping, backflips and spinning.

153. Annex III of the Directive states:

‘3.3 Establishments shall have appropriate enrichment techniques in place, to extend the range of activities available to the animals and increase their coping activities including physical exercise, foraging, manipulative and cognitive activities, as appropriate to the species.

Furthermore, in the species-specific section:

6. Non-human primates

The environment shall enable non-human primates to carry out a complex daily programme of activity. The enclosure shall allow non-human primates to adopt as wide a behavioural repertoire as possible, provide it with a sense of security, and a suitably complex environment to allow the animal to run, walk, climb and jump.

154. The UK NC3Rs 49 says this:

‘There is a great deal of published information on the housing and husbandry of non-human primates. The underlying principle is to provide safe, comfortable and hygienic accommodation and care, which allows the animals to perform a wide range of species-typical behaviour and exercise a degree of choice and control in their environment (e.g. to choose to socialise with, or avoid, group mates)’.

49 https://www.nc3rs.org.uk/housing-and-husbandry-non-human-primates
155. A comparison table of what the NC3Rs suggest are the components of a good primate housing system and those adopted at LPT:

<table>
<thead>
<tr>
<th>NC3Rs recommendations</th>
<th>LPT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Housing in stable, compatible groups (pairs at least).</td>
<td>Some monkeys in single housing</td>
</tr>
<tr>
<td>Adequate socialisation and habituation to humans, and training for cooperation with husbandry and procedures, where appropriate.</td>
<td>No evidence of training, certainly none with positive reinforcement</td>
</tr>
<tr>
<td>Sufficient space to provide for exercise, a range of species-typical behaviours, structural division of the enclosure, and suitable environmental enrichment.</td>
<td>Some monkeys in cages below legal requirement, cages generally barren</td>
</tr>
<tr>
<td>A solid floor as a resting area and to allow provision of substrate for foraging.</td>
<td>Cage floors were bars. No foraging material provided.</td>
</tr>
<tr>
<td>Sufficient enclosure height to allow vertical flight if alarmed; no small double-tier cages since these limit upward movement and therefore can be stressful for the animals. Evidence suggests the lower levels can be dark and the animals may receive less attention from staff.</td>
<td>Some monkeys were housed at ground level in two tier systems preventing flight</td>
</tr>
<tr>
<td>Structures to enable utilisation of as much of the enclosure as possible (i.e. to increase the useable space for the animals), for example, perches, platforms, swings, ropes, ladders; sufficient for all animals to occupy without competition</td>
<td>No structures except the bar themselves, with the exception of viewing balconies for some monkeys</td>
</tr>
<tr>
<td>Visual barriers to allows animals to control their social interactions</td>
<td>No visual barriers</td>
</tr>
<tr>
<td>Nest areas for species that use them (e.g. wooden nest boxes and plastic hanging buckets for marmosets and tamarins)</td>
<td>No nest boxes</td>
</tr>
<tr>
<td>A varied diet appropriate for the species</td>
<td>A small piece of fruit provided only twice a week</td>
</tr>
<tr>
<td>The ability to forage, including appropriate artificial feeding devices and scatter feeding</td>
<td>There were no opportunities to forage.</td>
</tr>
<tr>
<td>Appropriate wood (i.e. no chemical preservatives or long strips that can block the gut) for species that gnaw (e.g. marmosets) and for scent-marking</td>
<td>N/a</td>
</tr>
<tr>
<td>Toys, chews, tactile materials and destructible materials (e.g. cardboard boxes) to provide a degree of control over the environment.</td>
<td>No such materials were provided.</td>
</tr>
<tr>
<td>Adequate light levels and appropriate spectral emission for species' needs.</td>
<td>No natural lighting</td>
</tr>
<tr>
<td>A flexible enclosure/furniture layout to allow stress-free capture.</td>
<td>No</td>
</tr>
<tr>
<td>Provision to facilitate positive reinforcement training in groups (e.g. separate areas in front of the cage where dominant and subordinate animals can be trained simultaneously).</td>
<td>No</td>
</tr>
<tr>
<td>A degree of novelty (e.g. minor changes in furniture, feeding practices, toys).</td>
<td>Very little was provided</td>
</tr>
<tr>
<td>Access to outdoors wherever possible.</td>
<td>No</td>
</tr>
</tbody>
</table>
Cats

156. Paragraph 3 of Section B of Annex III of the Directive states:

‘Cats shall not be single-housed for more than 24 hours at a time. Cats that are repeatedly aggressive towards other cats shall be housed singly only if a compatible companion cannot be found. Social stress in all pair- or group-housed individuals shall be monitored at least weekly. Females with kittens under four weeks of age or in the last two weeks of pregnancy may be housed singly’

157. Cats used in studies were sometimes housed singly at LPT for several days. For example, in study 36897 cats were housed singly for at least 13 consecutive days.

Rabbits

158. A group of around 24 rabbits were individually housed in small metal cages in what appeared to be a basement and/or storage room. There were two structures, each containing cages, four across and three down. It was very dark area with limited lighting and the design of the cages (with a large metal feeder and water bottle attached to the outside of each cage) meant that the rabbits must have been living in the dark all day and all night.

END OF REPORT