Agenda – NC3Rs Primate Welfare Meeting 2005

09.30	**REGISTRATION and COFFEE**
10.00 – 10.10	**Welcome and introduction**
10.10 – 10.30	**Primate training – a UK survey** *Dr Mark Prescott, NC3Rs*
10.30 – 10.50	**Training of macaques used in neuroscience research** *Anon, UCL Institute of Neurology*
10.50 – 11.10	**Training macaque monkeys for food reward** *Anon, University of Oxford*
11.10 – 11.30	**Good practice for socialisation of macaques** *Mrs Sarah Wolfensohn, University of Oxford*
11.30 – 11.50	COFFEE
11.50 – 12.10	**Training of primates used for regulatory toxicology studies** *Anon, Covance Laboratories*
12.10 – 12.30	**Training marmosets for capture: methods, time investment, selection, and impact on welfare** *Ms Verity Bowell and Dr Hannah Buchanan-Smith, University of Stirling*
12.30 – 12.50	**Clicker training of cynomolgus macaques in Sweden** *Dr Mats Spångberg, Swedish Institute for Infectious Disease Control*
12.50 – 13.00	**DISCUSSION**
13.00 – 13.50	**LUNCH**
13.50 – 14.00	**Introduction to afternoon break-out groups** *Dr Mark Prescott, NC3Rs*
14.00 – 15.00	**Break-out group discussions** **Group A – Socialising primates to humans** **Group B – Accommodation considerations for training** **Group C – Use of positive and negative reinforcement** **Group D – Managing health and safety implications** **Group E – Exploring costs and benefits to primates**
15.00 – 15.20	**COFFEE**
15.20 – 16.20	**FEEDBACK and CLOSE**

Primate training – a UK survey

Dr Mark Prescott
NC3Rs

Laboratory-housed non-human primates may experience a range of potentially stressful interactions with humans, including physical restraint, venepuncture, injection, catching and cage-change. Training the animals to co-operate using positive reinforcement is one means by which staff can significantly reduce or eliminate the adverse impact of such procedures and, therefore, is a refinement technique. Use of training can enhance not only animal welfare but also quality of science, because suffering in animals can result in physiological changes that are, at least, likely to increase variability in experimental data and, at worst, may invalidate research findings. I surveyed use of training in over half of UK establishments using and breeding primates, utilising a mixed-mode questionnaire. The survey demonstrated that there is widespread awareness of training as a refinement technique, and appreciation of its diverse benefits, but that training is not used as widely or as fully as it might be. This is due to real constraints (e.g. staff, time and a lack of confidence in ability to train), but also perceived constraints, which can be overcome through information sharing and education (e.g. supposed lack of information on how to train, and overestimation of the time investment needed). There is also variation between establishments in the purposes of training and the techniques used, with a reliance on negative reinforcement in some. I conclude that there is considerable scope for refinement of common scientific, veterinary and husbandry procedures through use of positive reinforcement training, and refer to some resources designed to help establishments take action.

Training of macaques used in neuroscience research (movement)

Anon
UCL Institute of Neurology

Our main interest is in the control of skilled hand movements by the brain and is prompted by the need to understand why hand and finger movements are particularly affected by damage to the cortex, and its major descending pathways, for instance as a result of stroke, spinal injury or cerebral palsy. Much of the work involves the use of experimental primates, since these provide the best available model for the human sensorimotor system controlling the hand. We are now focusing on visually-guided grasp and manipulation of objects. We are studying the brain mechanisms in the premotor cortex that allow visual information about objects to select the appropriate motor commands that allow grasp and manipulation appropriate to the size and shape of the object. This transformation appears to depend upon a close interaction between premotor and primary motor cortex.

I shall touch on several aspects of our research programme, including monkey species, numbers used and selection of animals and pair-housing regimes. I will give a detailed description of our training regime, which is currently based on solid food rewards, but which is designed to use water rewards as additional reinforcement. I will also focus on refinement/reduction issues which include use of MRI to improve implant technology and guide neurophysiological recordings, the use of multiple electrode recordings to improve data yield per monkey, and the use of an antimitotic compound, 5FU, to reduce the problem of dural scarring for transdural microlectrode penetrations. I will also describe pre- and post-operative care and recent improvements for both EMG and headpiece implants.

Training macaque monkeys for food reward

Anon
University of Oxford

Training macaque monkeys for food reward is not in itself a regulated technique under the Animals (Scientific Procedures) Act, so long as the animals are not physically restrained and are not deprived of their normal food intake. All of the methods I am familiar with meet both these requirements. However, when training is part of a procedure that is regulated for some other reason, for example in a cognitive neuroscience experiment where the purpose of training is to measure the effect of a specific brain alteration upon some specific cognitive ability, then the technique of training becomes one to which the 3Rs can legitimately apply. The aim, in such a case, should be to design the training protocol so as to maximize its accuracy in measuring the cognitive ability that is to be tested. By reducing error variance in the experimental measure, this will minimize the number of animals that need to be used. One important determinant of measurement accuracy in this context is simply the number of trials per day which each animal performs in the cognitive task. The more trials per day, the more stable and accurate the measurement. Thus, it is not desirable in general to use only highly palatable foods such as grapes or Smarties as rewards, since the animals will receive an unbalanced diet if they are given many trials per day with these rewards. A better strategy is to allow the animal to receive as food rewards in the experimental task the same balanced diet that the animal would receive in the home cage if it was not being tested. This can be achieved by giving pellets of proprietary monkey diet on many trials in a test session, and finally giving a single large reward, consisting of mash with fruit, nuts and other supplementary foods according to the individual animal's preference, as the last reward in the test session. Using such a regime of food reward, the animals can be shown experimental stimulus material, usually though not necessarily consisting of visual stimuli displayed on a computer-controlled monitor, their responses to those stimuli can be detected by various devices including, most commonly, a touchscreen, or a joystick, or a non-invasive eye tracker, and these responses can be rewarded in such a way as to elicit the desired measurement of the target cognitive ability. Accurate and stable measurements can then be taken before operation as well as after, in order to allow for differences among individual animals in their pre-operative ability.

Good practice for socialisation of macaques

Mrs Sarah Wolfensohn
University of Oxford

The Oxford English Dictionary definition of socialisation is "The process of forming associations or of adapting oneself to them; especially the process whereby an individual acquires the modifications of behaviour and the values necessary for the stability of the social group of which he is or becomes a member." Primates in the laboratory are required to modify their behaviour to adapt themselves to the close proximity in which they find themselves to human beings. These people may be acting as caretakers, researchers or veterinarians, but all will prefer an animal that responds appropriately to their presence. Achieving the appropriate effect on behaviour and the stability of the social group is critical to the successful outcome of the research, both in terms of the quality of the scientific data and the optimisation of the animals' welfare and application of the 3Rs. The presentation will consider when and how to effect this process and what factors should be taken into account in the development of a socialisation programme to achieve the desired outcome. Video clips will be used to illustrate the modification of behaviour in different situations.

Training of primates used for regulatory toxicology studies

Anon
Covance Laboratories

Over recent years significant progress has been made in both the housing and sourcing of macaques used for regulatory toxicology studies. Housing has progressed from small, individual, barren, metal cages, providing little stimulation or enrichment, to large complex pens allowing permanent gang-housing, foraging and other enrichments. Sourcing of animals has also progressed from wild-caught animals of unknown or unreliable health status and provenance through dealers, to purpose-bred, high health status animals provided by a select number of established breeding centres approved by the UK Home Office. Whilst progress can still be made in these areas it is arguably recognised that the most significant strides in the welfare of primates used on regulatory toxicology studies are now to be made in refinement of procedures, particularly in the areas of training, habituation and co-operation. Much has been written and shared regarding the training of macaques used in academic/behavioural and fundamental research settings (often involving singly-housed animals). However, little progress appears to have been made regarding the training of animals used in the short-term and busy environment of regulatory toxicology studies using gang housed animals or otherwise. The regulatory toxicology macaque has very different demands placed on it to those involved in other areas of less intensive study, particularly in terms of the duration, intensity of study and numbers of animals involved which present significant challenges to the provision, efficacy and potential benefits of training. At Covance, whilst still in the early stages regarding training, we have made some progress with Mauritius origin cynomolgus monkeys *(Macaca fascicularis)*, particularly regarding co-operation with handling and husbandry procedures which has encouraged further efforts.

Training marmosets for capture: methods, time investment, selection, and impact on welfare

Ms Verity Bowell and Dr Hannah Buchanan-Smith
University of Stirling

Laboratory housed primates are subject to a range of stressful experiences both as a result of their husbandry regimes and the experimental procedures in which they are used. Increasingly Positive Reinforcement Training (PRT) is being identified as a possible way of reducing this stress, and improving the quality of life for laboratory housed primates. Most of the research to date has involved training of either chimpanzees or macaques, with much less on New World primates, of which common marmosets are the most frequently used in the UK. Forced restraint is known to be extremely stressful, and to impact on physiology and biochemistry, and subsequently on the validity of the science. Marmosets can be trained to cooperate with a variety of tasks and two methods of training marmosets to cooperate with capture will be discussed in detail; training to enter a transport box, and training to accept hand capture. The methods and time investment to train these tasks will be described. Data will be presented to illustrate how monkeys can be selected to improve training success, and to show the impact that training has on coping with challenges. The welfare implications of such selection will also be considered, and recommendations for good practice made.

Clicker training of cynomolgus macaques in Sweden

Dr Mats Spångberg
Swedish Institute for Infectious Disease Control

At the Swedish Institute for Infectious Disease Control cynomolgus macaques are used for HIV vaccine and therapeutics research, malaria vaccine studies, neurological research using brain imaging with PET, and for other purposes. The facility, which was inaugurated in 2003, is a 7,000 m^2 building, meant primarily for housing non-human primates up to and including biosafety level (BSL) 3. A section of the building is also designed for housing rodents, rabbits, etc.

Rigorous Swedish requirements for non-human primate care and use greatly influenced the design of the building. All primate rooms are equipped with large windows, providing daylight to the animals. The primates are kept in pairs or small groups, and the minimum cage size for a pair of macaques in the BSL-3 area is 2 m^2 floor area and a height of 2 m. The cages are environmentally enriched and a balcony box is incorporated for easier handling and training of the animals. Primates kept under conventional conditions are housed in groups of five to seven animals, in large rooms with access to outdoor pens.

We train the macaques using positive reinforcement, utilizing a clicker as an instrument to bridge between the correct behaviour and the reward (conditioned reinforcer). The clicker helps the animal to understand which behaviour is the desired one, and is used to shape different behaviours such as sitting at a target, sitting for injection, presenting the hands and opening the mouth for clinical inspection, etc. All animal caretakers are educated to perform the clicker training, and strict shaping protocols are used for the different behaviours. The program is supervised by an ethologist, who also gives lectures to the personnel and gives advice if problems appear in the training of individual animals. Each step in the training is carefully documented in records, and when a behaviour is fixed it is often possible for other caretakers to ask the animal to perform the behaviour.

During the presentation, examples of clicker training in different situations will be shown on video, and potential problems and solutions will be discussed. The problem of handling animals participating in experiments before they are fully trained will also be addressed.

Break-out groups – NC3Rs Primate Welfare Meeting 2005

Group A- Socialising primates to humans

- How do you socialise primates to humans? Is it better to have a formal rather than *ad hoc* socialisation programme?
- Is it necessary to enter animals' cages in order to socialise them to humans? What advantages and disadvantages does this have compared with interaction through cage bars?
- When is the best time to socialise primates (e.g. before or after weaning)? What is the benefit of socialisation for the animals?
- Is it practical to conduct temperament assessments to assign animals to research projects with the goal of obtaining the best candidates for those studies? Is this already being done? If not, why not?
- Is there scope for habituating animals at the breeding centre to objects that they may encounter later in life (e.g. syringe, restraint chair, stethoscope)?

Group B- Accommodation considerations for training

- What cage adaptations can me made to facilitate training (e.g. verandas)? Try to formulate a list of accommodation considerations for successful training (e.g. a location with minimal disturbance).
- How do accommodation considerations for training differ between breeding and experimental units (e.g. macaque breeding groups may consist of one adult male and 12 adult females – this is a large group to manage during training)?
- Does provision of environmental enrichment (e.g. play areas) affect training success in any way? If there are issues, how might they be addressed?
- Is there an optimal group size for training? For example, is training more effective when animals are in pairs or groups?
- Have you used 'reward zones' or target training as a means of separating animals to minimise aggression during training and increasing training effectiveness?

Group C - Use of positive and negative reinforcement

- What training goals do you have for your primates and how are these achieved (e.g. what reinforcers or "threats/punishments" are used)?
- Under what circumstances is negative reinforcement the first option for training animals?
- Hypothetically, what would be the impact of research if only positive reinforcement could be used? What are the benefits of only using negative reinforcement?
- How do you manage individual differences in training performance (e.g. have you tried different reinforcers to motivate different animals, do you collect data on each animal's progress)?

- How can you ensure sufficient time for training staff and animals before studies begin (e.g. could daily work routines be better organised to allow for training)?

Group D- Managing health and safety implications

- What are your health and safety concerns about training primates and how have you been able to address these? Do you think health and safety professionals are sufficiently educated on the risks involved and their management?

- Do the primates in your care associate the presence of certain individuals with positive or negative experiences? How can you get the animals to view these people in a more positive manner?

- What in your laboratory do the primates find fearful and how do they react? How have you tried to change undesirable animal behaviour (e.g. through socialisation, by enriching the laboratory environment)?

- Do you think your understanding of primate behaviour is good, or is there scope for improvement? What kinds of resources would assist you to predict your primates' actions and thus reduce the risk of injury, or to communicate with the animals more effectively during training?

Group E - Exploring costs and benefits to primates

- It is often claimed that training for performance of some cognitive or behavioural task is enriching, but what evidence exists to substantiate this claim? If such training is enriching, what are the consequences, in terms of animal welfare, of stopping the test when the experiment or study ends or during weekends/holidays, and how might these be addressed?

- What impact might training one primate/group by rewarding it with treat foods have in the colony room (e.g. increased aggression)? What can be done to reduce/avoid any welfare costs to the animals?

- Bad training (e.g. using punishment, reinforcing the wrong behaviour, or being inconsistent – either within or between trainers) may lead to frustration, lack of cooperation and management problems from the animals. What solutions might be used to prevent bad training occurring?

- Trained primates are valuable to research programmes and, given the relatively long lifespan of primates, may be used for many years. However, long-term maintenance in the laboratory and use in further procedures can entail significant welfare costs. How long should trained primates be used for and what criteria would you consider grounds for euthanasia or retirement?