LASA 3Rs Section/UFAW Meeting
6th September 2016

Planning and implementing the 3Rs: Strengths, Weaknesses, Opportunities and Threats

~ PROGRAMME ~

GlaxoSmithKline R&D,
Medicines Research Centre,
Gunnels Wood Road,
Stevenage, Herts.

LASA has awarded this meeting 5 CPD points

Programme

10:00-10:40	Arrival, coffee and registration
10:40	Welcome & introduction
	Session 1– Chair, Robert Hubrecht
10:45-11:15	**Directive 2010/63/EU as global standard for animal facilities** Jan Lund Ottesen, Novo Nordisk
11:15-11:45	**Bricks, mortar, people and culture – creating a new facility from the perspective of the NTCO** Alan Palmer, Francis Crick Institute
11:45-12:15	**Application of the 3Rs: Challenges of introducing reduction and refinement through advanced imaging** Mike Dennis, Public Health England
12:15-13:30	Lunch and networking
	Session 2– Chair, Patricia Pimlott
13:30-14:00	**Rederiving the Crick: The challenges and successes of a large-scale multi-site, multi-species, multi-Institute project** KE Mankelow, Francis Crick Institute
14:00-14:30	**Working with universities to support 3Rs implementation** Mark Prescott, National Centre for the Replacement, Reduction and Refinement of Animals in Research (NC3Rs)
14:30- 15:00	Coffee/tea
	Session 3– Chair, Joanna Cruden
15:00-15:30	**R2 and the Avoidance of Unnecessary Suffering** Manuel Berdoy, University of Oxford
15:30-16:00	**Systematic reviews of animal studies – how they can promote the 3Rs and more** Judith van Luijk, SYRCLE, Radboud University Medical Center
16:00	Final comments and close of meeting

Abstracts

Directive 2010/63/EU as global standard for animal facilities
JL Ottesen, Laboratory Animal Science, Novo Nordisk, Denmark
jlo@novonordisk.com

Directive 2010/63/EU is acknowledged to be one of the most strict legislations in the world with regard to requirements for accommodation of laboratory animals and many see this as a challenge when building animal facilities outside EU. If your animal facility is located in EU it goes without saying that it has to live up to the Directive, however, when planning new facilities or upgrades to old ones outside EU this could also be seen as an opportunity.
First of all it is an opportunity for the animals to get better housing (and care) conditions. The implemented standards for housing animals at Novo Nordisk have significantly improved the welfare of the animals. The standards take the physiological and ethological (behavioural) needs of the animals into consideration and are based on valuable input from ethologists and the animal caretakers. Improvements include group housing of rabbits in large pens, larger cages and hides for the rodents and large exercise areas for the dogs and pigs.
Attitudes towards animals vary with national perceptions and regulation. Novo Nordisk has therefore established a set of principles and global standards for the housing and care of animals and internal guidelines that as a minimum follow Directive 2010/63/EU but in many cases exceeds this.
To ensure that the company's global standards are applied globally, internal training of employees working with animals (e.g., veterinarians, laboratory technicians, and animal caretakers) is conducted across Novo Nordisk's global sites and a staff exchange programme for employees from different sites has been established.
Beside the benefits for the animals employees also prefer to work with animals housed under improved conditions so there is also an opportunity when it comes to talent attraction.
The presentation will include examples from the process we go through when planning new facilities or upgrades to old ones including those that affect building in countries outside EU.

Bricks, mortar, people and culture – creating a new facility from the perspective of the NTCO
Alan Palmer NTCO, Biological Research Facility, Francis Crick Institute, London

On the 1st April 2015 the Francis Crick Institute was officially formed from two established research centres, the MRC National Institute for Medical Research and CRUK's London Research Institute. Whilst the new facility in London NW1 were still some eighteen months from practical completion at this point, and split over three legacy sites, the formal merger posed many challenges and opportunities with regard to staff training, awareness, communications and engagement. This presentation looks at some of these opportunities and challenges from the perspective of the NTCO in defining a new single working culture for a new Institute.

Application of the 3Rs: Challenges of introducing reduction and refinement through advanced imaging
Mike Dennis, Public Health England

In-life imaging of animals challenged experimentally with infectious agents greatly enhances the quality of data gained from a pathogenesis or efficacy study. This additional information also presents an opportunity to address ethical issues by refining the studies and reducing the number of animals used. Both magnetic resonance (MR) and computed tomography (CT) imaging modalities are used extensively in human medicine to diagnose disease and to monitor the efficacy of treatments. To make animal-based studies as relevant as possible to the clinical situation, such technologies should be applied wherever possible. Imaging animals infected with disease- causing agents presents a number of challenges for the protection of staff as well as the well-being of the animals during the scanning process. This presentation will address the challenges and benefits of using mobile scanners for imaging non-human primates infected with tuberculosis and how reduction and

refinement outcomes have been achieved whilst maintaining staff safety and increasing operational flexibility.

Rederiving the Crick - The challenges and successes of a large-scale multi-site, multi-species, multi –Institute project

KE Mankelow, S Hart-Johnson, I Rosewell, KE Mathers, Genetic Manipulation Services, The Francis Crick Institute, London, UK
Katharine.Mankelow@crick.ac.uk

In 2014, MRC and CRUK began a 24-month programme to rederive in excess of 1350 mouse strains in advance of closing two existing research institutes – National Institute of Medical Research (NIMR), Mill Hill and Cancer Research UK – London Research Institute (CRUK-LRI), North and central London; both contributing institutes to the Francis Crick Institute. This was done via an intermediate health-screened animal facility at Poplar Block, Clare hall, Hertfordshire. In light of the increasing evidence of the effect of the microbiota on phenotype, we undertook a comprehensive analysis of the metagenome of animals at several commercial breeders as well as at the former NIMR and LRI, to both provide a baseline of the microbiota within all donor units, and to help us identify suitable recipients.
We are now in the final stages of the rederivation process – in 2016 the mass expansion of mouse lines began, and we are now migrating strains to the new Francis Crick Institute site at St. Pancras, Central London. To manage these lines, we have chosen the "Mouse Colony Management System" (MCMS) developed for the Wellcome Trust Sanger Institute, which allows us to manage breeding, track pedigrees, manage cryopreserved stock, monitor health concerns and also regulate and monitor experimental cohorts.
In this presentation, I will outline some of the challenges and successes we have experienced during this large-scale rederivation process. Throughout we have tried to reduce and refine animal use wherever possible. Two ways in which we have done this are through the use of genetically sterile Prm1 Tg mice to provide all embryos transfer recipients, and by using the Paratech NSET device to transfer embryos non-surgically without the need for anaesthesia wherever possible. We have also improved out aseptic surgical techniques in line with the latest national and local guidelines and advice.

Working with universities to support 3Rs implementation

MJ Prescott, National Centre for the Replacement, Reduction and Refinement of Animals in Research (NC3Rs)
mark.prescott@nc3rs.org.uk

Universities and other public bodies account for approximately 60% of the ~4 million procedures conducted on animals annually in the UK. Academia is therefore an important sector for the NC3Rs. In our first 10 years, our primary focus has been on increasing the engagement of individuals in the 3Rs and collaborating with the organisations that fund, regulate or represent them. We have attracted thousands of academic scientists to apply for 3Rs research funding, and invested over £60 million into university-based research, career development, infrastructure and open innovation, delivering 3Rs and other impacts. We have worked with universities on, for example, the adoption of our ARRIVE Guidelines to improve the reporting of *in vivo* studies, organisation of institutional 3Rs symposia, and hosting of our Summer School for PhD students. Our input into the peer review processes of the major UK bioscience funding bodies, events and online training resources, have helped apply the 3Rs to individual experiments. In Our Vision 2015-2025, we committed to more directly support institutions to implement a culture that actively promotes the 3Rs and engages staff at all levels of responsibility. This followed extensive consultation with university staff who reported that more can and should be done to support an active 3Rs community within their establishments. To deliver our commitment, we have appointed Regional Programme Managers, co-funded by the NC3Rs and university consortia, who work within the universities to: i) provide expert advice and disseminate the work of the NC3Rs, ii) support named persons working under the ASPA with the latest information on the 3Rs, iii) horizon scan for research and technologies with 3Rs potential and connect them with potential end-users, and iv) facilitate improved knowledge exchange across institutions. To complement these new roles, we have developed a self-assessment

tool to allow higher education institutions to benchmark their 3Rs activities and progress in six key areas, with a second shorter tool for individual research groups. The intention is to launch these tools as interactive, secure online resources with the functionality to map scores and provide guidance on how improvements can be made. Finally, recognising the importance of inculcating a 3Rs-minded approach early in the careers of researchers and animal technologists, we have also developed new resources for use in the training of prospective licensees, including a video tutorial on the scientific importance of the 3Rs and the support the NC3Rs provides to the scientific community.

R^2 and the Avoidance of Unnecessary Suffering
Manuel Berdoy, University of Oxford.

Since regulated procedures have a crucial welfare component, the waste of lives through bad experimental design is unnecessary suffering. Experimental Design in biology is mostly about logic, common sense and the systematic application of relatively simple techniques to produce un-biased experimental results. This is good news because this should be relatively straightforward. Yet this is where the biggest blunders continue to be made in the fields of Biomedical Sciences, with expensive consequences on results and ultimately, suffering.

I aim to address some of the essential principles, indeed inescapable laws, that are behind designing a good animal experiment, the traps in which we have all fallen into, possible hopes and new resources on the horizon (e.g. the EDA) that can help in that journey, all in a very much "reduced" session where I hope that words "enjoyment" and "statistics" can belong in the same sentence, at least sometimes.

Systematic reviews of animal studies – how they can promote the 3Rs and more.
Judith van Luijk, SYRCLE, Radboud University Medical Center

Abstract pending…