



RSPCA ERP Lay Members' Forum 2012



RSPCA ERP LAY MEMBERS' FORUM 2012

Tuesday 11th December 2012, The Royal Society

Chair: Maggy Jennings

10.30 Registration and coffee

11.00 Welcome and introduction

Transposition of the EU Directive into UK law

11.05 Transposition of the Directive into UK law: summary of what is to happen and how it impacts on the ERP

David Buist and Anne-Marie Farmer, Home Office

11.35 Q&A/discussion session

11.50 The importance of severity classification under the new Directive: what the new requirements will mean for the UK

David Anderson, European Commission

12.10 Q&A/discussion session

12.20 Views from the animal care staff and Named Persons perspective

Ken Applebee, Kings College London

12.40 Animal Welfare and Ethical Review Bodies (AWERBs) and the new National Committee (NC): opportunities and challenges

Jane Smith, Boyd Group

12.50 Gathering ideas on AWERBs and the NC (to continue over lunch)

13.00 Lunch

Implementing animal welfare and the 3Rs in practice

14.00 Animal needs and animal welfare

Robert Hubrecht, Universities Federation for Animal Welfare (UFAW)

14.20 A practical case study: applying the 3Rs to nausea and vomiting research

Paul Andrews, St George's, University of London

14.40 Focus on GA animals: have passport, will travel!

Kathleen Mathers, National Institute for Medical Research (NIMR)

15.10 Summary of 'gathering ideas session' and AOB

15.30 Close

Transposition of the Directive into UK law: a summary of what is to happen and how it will impact on the ERP

David Buist and Anne-Marie Farmer, Home Office

This presentation will provide an overview of the similarities and differences between the current UK regulations and the requirements of the new EU directive as they will be implemented by the Animals (Scientific Procedures) Act 1986 Amendment Regulations 2012. Changes that impact directly and indirectly on the ethical review process and its transition to an Animal Welfare and Ethical Review Body (AWERB) will be reviewed in more detail.

Finally, the mandatory composition and functions of the AWERB will be compared with those of the current ERP and the presentation will conclude by exploring how, and to what extent, current beneficial elements of the ERP that will not be mandatory might be retained.

The importance of severity classification under the new Directive: what the new requirements will mean for the UK

David Anderson, European Commission

Directive 2010/63/EU regulating scientific procedures on animals, has introduced a number of requirements which are new to many member states. To assist member states and the scientific community with implementation of the Directive, the Commission has hosted a series of Expert Working Groups (EWGs) to prepare some additional guidance on certain aspects of the Directive, such as statistical reporting, education and training and retrospective severity assessment. The latter is the subject of this presentation. General recommendations from the Expert Working Group were agreed by the member states earlier this year, and the group continues to work on preparing some illustrative examples of the “severity process”.

The Directive requires that a *prospective* assessment is made of the severity of each procedure in a project and that a *severity classification* is assigned. This may be either “non-recovery”, “mild”, “moderate” or “severe”. An annex to the Directive (Annex VIII) provides guidance on the factors to be taken into account in the consideration of *prospective* severity and provides some examples in each severity category.

In addition, there is a new requirement that the *actual severity* of the pain, suffering, distress or lasting harm *experienced by the animal* must be reported for publication in the annual Home Office statistics. At present, only the *prospective assessment* of severity of the *project* (as opposed to procedures), made at the time of the project evaluation is reported. The actual severity of any previous procedures will also be a key consideration in determining whether or not an animal can be *re-used* in further procedures.

Prospective review of project proposals and classification of severity are new requirements for many member states, providing opportunities to improve the quality of science and welfare throughout the EU. The reporting of the actual suffering experienced by the animals should provide greater transparency and understanding of the impact of scientific procedures on animal welfare.

However, a common understanding of severity and a consistent approach to assessment is necessary to promote a level playing field for scientists (and animals) and to generate meaningful statistical reports. The Animal Welfare and Ethical Review Body (AWERB) in the UK is ideally placed to promote a common approach to severity at an establishment level.

Views from the animal care staff and Named Persons perspective

Ken Applebee, Kings College London

Named Animal Care and Welfare Officers (NACWOs) have a pivotal role to play in the Local Ethical Review Process (LERP), which will be known from 2013 as the Animal Welfare and Ethical Review Body (AWERB).

For many NACWOs it may be an extremely difficult transition from the animal facility to what is often a formalised committee environment. Some NACWOs may feel uneasy dealing with specialist scientific jargon or extremely complex experimental protocols. However, given the opportunity and with encouragement, NACWOs have a wealth of experience and can contribute in their own area of expertise, namely the care and welfare of animals in science and its contribution to refinement.

I will provide some insight into what motivates the animal care staff and NACWOs in particular. Also I will illustrate a number of similarities between NACWOs and Lay Persons on the LERP.

Finally I will touch on how NACWOs can work within a team including Named Veterinary Surgeons, Certificate Holders, and of course Project and Personal Licence Holders.

Animal Welfare and Ethical Review Bodies and the new National Committee: opportunities and challenges

Jane Smith, Boyd Group

Current UK regulations provide two specific opportunities for external input, including lay perspectives, in matters related to the care and use of laboratory animals: (i) at an institutional level, via local ERPs; and (ii) at a national level, via the Animal Procedures Committee (APC) - both of which are set to change in response to requirements under the new EU Directive.

The new *Animal Welfare and Ethical Review Bodies* (AWERBs) will have to carry out the tasks listed in the Directive, which are broadly similar to the functions of existing ERPs - see Box 1 below. The APC will be replaced by a new *National Committee for the Protection of Animals Used for Scientific Purposes* (NCPASP), which will have the functions shown in Box 2. Membership of the Committee is not yet specified.

Box 1

AWERB tasks

- Advise staff on matters related to animal welfare (supply, accommodation, care and use)
- Advise and keep staff informed on the application of the Three Rs
- Establish and review processes for monitoring, reporting & follow-up on animal welfare
- Follow the development and outcome of projects
- Advise on re-homing schemes

Box 2

NCPASP functions

- Advise the Home Office and AWERBs on acquisition, breeding, accommodation, care and use of animals and ensure sharing of best practice
- Exchange info on operation of AWERBs and project evaluation and share best practice within the EU
- *No details of membership*

This session (to be concluded at the end of the Forum) will provide an opportunity to discuss the opportunities and challenges afforded by these new arrangements, and in particular to gather thoughts and ideas on:

- (i) What lay people hope the new national Committee will achieve (including how it should relate to AWERBs); and
- (ii) How, as we move to AWERBs, current ERP practices might be developed, to enhance their effectiveness and efficiency.

Animal needs and animal welfare

Robert Hubrecht, UFAW

Animals used in research should be kept in conditions that as far as possible meet their needs and provide good welfare. This is required by legislation (UK and European Directive 2010/63/EU), is necessary on ethical grounds and advisable on scientific grounds as data collected from the animals is less likely to be biased by stress and show less variability. Animal needs are the product of evolution, experience and selection, and establishing them often requires high-quality research to avoid the perils of uncritical anthropomorphism.

Assessing welfare also requires expertise, and while various measures can be used to inform welfare decisions, assessing an animal's welfare is just that - an assessment. Husbandry decisions should be informed by knowledge of animals' natural history but provisions do not necessarily need to be naturalistic. Members of the ERP can contribute to an institutions animal care standards by taking an active interest, visiting the animal unit, and asking questions about animal care and sourcing and staff training.

References

1. Hubrecht, R. & Kirkwood, J. (eds.) (2010) *The UFAW Handbook on the Care and Management of Laboratory and Other Research Animals*, Oxford, Wiley-Blackwell.
2. Young, R. J. (2003) *Environmental Enrichment for Captive Animals*, UFAW Animal Welfare Series, Oxford, Blackwell.

Applying the 3Rs to nausea and vomiting research

Paul L. R. Andrews, St George's, University of London

Nausea is an unpleasant sensation associated with the urge to vomit [1]. Vomiting is a reflex in which the stomach contents are forcibly ejected via the mouth. Rodents and rabbits are incapable of vomiting, but other laboratory mammals (e.g. dogs, ferrets) can vomit just as humans do - hence vomiting can be studied directly in animals [2]. Nausea, on the other hand, is a sensation that is difficult to identify even in other humans, except through verbal description.

This means that animal studies must rely on indirect methods to detect nausea (e.g. behaviour and/or chemical 'markers' in blood samples), working on the *assumption* that animals experience a sensation similar to nausea in humans [1,3]. Nausea and vomiting are generated by the brain in response to nerve signals from the gut (e.g. due to presence of toxins in food, some drugs) or the balance system in the ear (e.g. motion sickness), and also as a result of the impacts of certain drugs on the brain itself (e.g. opiates such as morphine).

As the above discussion suggests, nausea and vomiting (N&V) are both complex 'whole body' responses to specific stimuli. For this reason, it might be assumed that scientific studies of N&V will *necessarily* require 'whole bodies' - human or animal - and that replacement by other methods will be very difficult or impossible. However, in recent years, there has been progress in developing imaginative alternative approaches (encompassing all 3Rs), even in this challenging area.

Why study N&V?

The aims of animal experiments in this area, which involve experimentally causing animals to experience N&V, include:

- identifying novel anti-emetic medicines to control N&V caused by, for example, anti-cancer chemotherapy or general anaesthesia (for human and veterinary use);
- understanding why some potential new medicines induce N&V as side effects, to help identify compounds that cause N&V as soon as possible in drug development, before human studies;

- identifying behavioural and chemical 'biomarkers' of nausea in animals, which may be an underestimated welfare issue in research and veterinary settings. Biomarkers could also be useful for patients who may be suffering from nausea but are unable to report it (e.g. in paediatrics).

3Rs approaches

An NC3Rs workshop that brought scientists together to think imaginatively and creatively about replacing animals in N&V studies proposed a number of non-animal approaches (both *in silico* (computer) and *in vitro* (test-tube) studies) which, in the early stages of development of new medicines, could be used to identify compounds likely to cause N&V and remove them from further development – so in turn reducing the number of compounds that may need to be studied in animals further down the development pipe-line [3]. Examples include development of:

- (i) a **predictive algorithm** for identifying compounds likely to cause N&V, based upon systematic analysis of literature [4,5] (though lack of human data to compare with animals hampers progress);
- (ii) using **social amoeba** (unicellular organism) to identify emetic, bitter or pungent- tasting molecules [6];
- iii) *in vitro* studies of **human gut tissue** to identify the effects of molecules implicated in nausea [7].

Also, as contributions to refinement:

- a) using **telemetry** in the established ferret emesis model, to study biomarkers of nausea used in humans (e.g. electrogastrogram [8]) and;
- b) **brain imaging** of humans experiencing nausea. These studies [9] have begun to identify the brain pathways that lead to nausea and will enable refinement and reduction of animal studies aimed at identification of novel anti-emetic drugs.

References

1. Stern, R. M., Koch, K. L., Andrews, P.L.R. (2011). Nausea: Mechanisms and Management. New York, Oxford University Press Inc. pp.462

2. Sanger, G.J., Holbrook, J.D., Andrews, P.L.R. (2011). The translational value of rodent gastrointestinal functions: a cautionary tale. *Trends Pharmacol. Sci.*, 32, 402-409.
3. NC3Rs workshop. Holmes, A. M., Rudd, J. A., Tattersall, F. D., Aziz, Q. & Andrews, P. L. R. (2009). Opportunities for the replacement of animals in the study of nausea and vomiting. *Br. J. Pharmacol.*, 157, 865-80.
4. Funded by NC3Rs & Pfizer Inc. See for example: Percie du Sert, N., Holmes, A. M., Wallis, R., Andrews, P. L. (2012). Predicting the emetic liability of novel chemical entities: a comparative study. *Br. J. Pharmacol.*, 165, 1848-67.
5. Percie du Sert, N., Rudd, J. A., Apfel, C. C., Andrews, P. L. (2011). Cisplatin-induced emesis: systematic review and meta-analysis of the ferret model and the effects of 5-HT(3) receptor antagonists. *Cancer Chemother. Pharmacol.*, 73, 667-86.
6. Project led by Prof. R. Williams at RHUL, UFAW funded; see also NC3Rs CRACK IT Solutions. Robery, S., Mukanowa, J., Percie du Sert, N., Andrews, P.L.R., Williams, R.S. (2011). Investigating the effect of emetic compounds on chemotaxis in *Dictyostelium* identifies a non-sentient model for bitter and hot tastant research. *PLoS one*, 6, e24439.
7. E.g. vasopressin. Study lead by Prof. G Sanger at QMUL. Broad, J., Andrews, P. L., & Sanger, G. J. (2012). Vasopressin contracts isolated human stomach: possible role in nausea? *Gut*, 61, A297-A298. doi:10.1136/gutjnl-2012-302514d.3
8. Percie du Sert, N., Chu, K. M., Wai, M. K., Rudd, J. A., Andrews, P. L. (2009). Reduced normogastric electrical activity associated with emesis: a telemetric study in ferrets. *World J. Gastroenterol.*, 15, 6034-43.
9. Project led by Prof. Q. Aziz at QMUL, funded by NC3Rs. Ng, K. S., Coen, S. J., Chua, Y. C., Ban, V. F., Gresty, M. A., Sanger, G. J., Andrews, P.L.R., Aziz, Q. (2012). Studies of the psychophysiological markers and the brain processing of nausea in healthy humans using a novel virtual reality video. *Gut*, 61, A317-A318. doi:10.1136/gutjnl-2012-302514d.51

Focus on GA animals: have passport, will travel!

Kathleen Mathers, Biological Services, MRC National Institute for Medical Research, London

The use of genetically altered (GA) animals, particularly mice, is now commonplace in the UK and worldwide. The generation, maintenance and use of these animals, however, continues to raise scientific, ethical and logistical questions as well as providing challenges in implementing the 3Rs.

Using case studies from a large academic establishment this presentation will explore a number of these challenges and some important questions with which ERPs are regularly faced. Opportunities for applying reduction and refinement through the sharing and archiving of GA mice will be discussed. Maximising the health and welfare of animals throughout their life by collating and disseminating relevant scientific and husbandry information in the form of databases and the use of 'mouse passports' will also be considered. Together these initiatives, which continue to need promotion and uptake will ensure that worldwide travel of mice does not diminish welfare and consistent standards of care are achieved in all establishments sending and receiving mice.

Notes ...



The RSPCA sees the involvement of lay perspectives as essential to the integrity of a successful ethical review process (ERP) and is committed to supporting and developing the role of lay members.

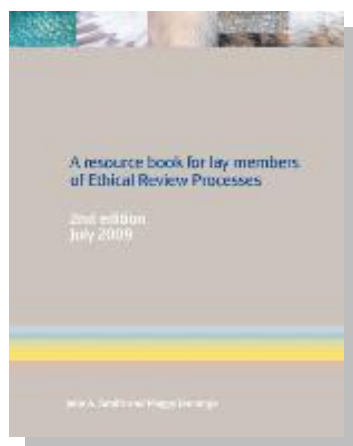
The research animals department organises an annual meeting for lay and other members of local ERPs. The meeting provides a forum for people to come together and share experiences of their work. They combine presentations on some of the many important issues that ERPs cover, with opportunities for group discussion.

For further information, see: www.rspca.org.uk/laymembers

... where you can download two useful resources:

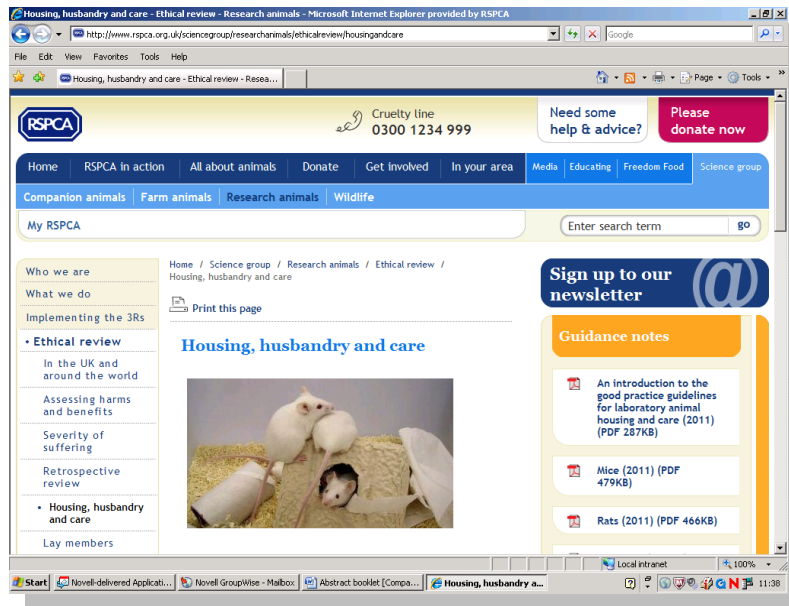
- **A resource book for lay members of Ethical Review Processes**, 2nd edition (2009). This is also available as a hard copy by emailing the address below.
- **Guiding principles on good practice for Ethical Review Processes**, 2nd edition (2010). This was produced by the RSPCA and Laboratory Animal Science Association (LASA) and sets out guidance on each of the seven functions of the ERP.

Both documents will be updated to take account of the revised EU Directive and its transposition into UK law from January 2013.



If you would like to register on our mailing list or have any questions regarding the ERP please email us at: erp-laymembers@rspca.org.uk

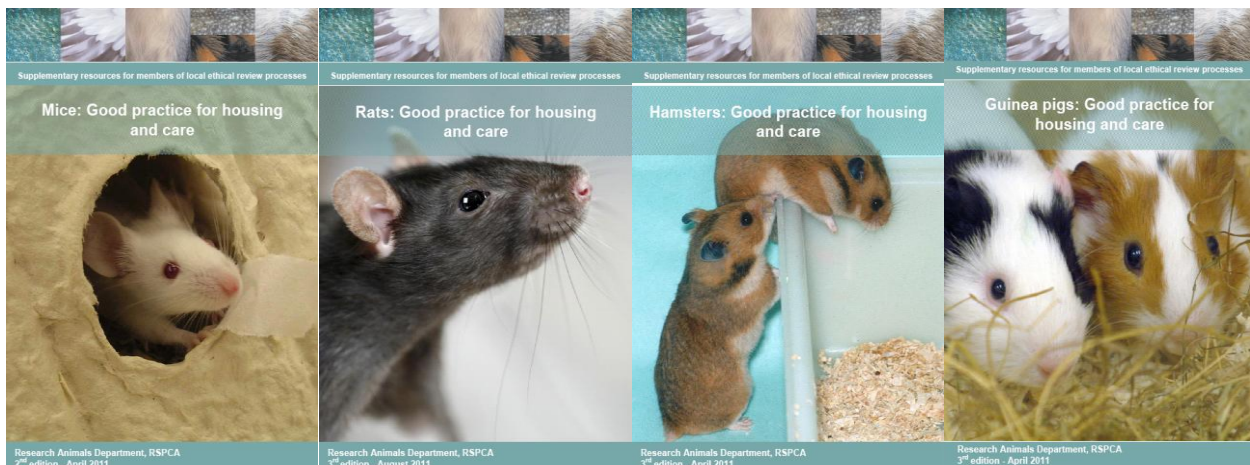
On the RSPCA website:



Our guidance notes on good practice for housing and care were all reviewed and updated in 2011 – all are free to download from the RSPCA website (URL on the left of this page). Species currently included are:

Mice	Rabbits	Cattle	Quail
Rats	Ferrets	Sheep	Pigeons
Hamsters	Dogs	Ducks and geese	Zebra finch
Guinea pigs	Pigs	Domestic fowl	<i>Xenopus laevis</i>

There is also information on **cage cleaning mice and rats** and **humane killing**, with more to come including **welfare assessment**, so please check our site regularly.





RSPCA ERP Lay Members' Forum 2012

