Session II-6: Setting limits and resolving conflicts between the Rs

Session II-6: Oral presentations

II-6-533

The 3Rs principle – mind the ethical gap!

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Over its 50 years of existence, the 3Rs principle has become a tremendous success. As an idea it is widely known and generally well accepted, it has made its way into many legislative texts and guidelines and it is often referred to in communication with the public and with potential critics of animal experimentation. The principle seems to unify the concern for better science with the concern for higher ethical standards. And the principle seems so clear and comprehensive that it is tempting to believe firstly that its full implementation is merely a practical and technical matter and secondly that once it is implemented it only takes good communication skills to achieve a wide public consensus about laboratory animal use. However, we think that both these beliefs are deceptive.

Firstly, we argue that underneath the seemingly clear surface of the 3Rs principle are both ambiguities and dilemmas which have clear ethical significance. Thus it is unclear what counts as reduction – is it in absolute or in relative numbers? Also the choice of species gives rise to questions in relation to refinement – is it always a refinement to move from a "higher" to a "lower" species? Between the 3Rs there are some obvious dilemmas. In fact, those working with the development and implementation of the 3Rs have more or less divided into two tribes – one focusing on replacement of live animal experiment and the other on reduction and refinement of actual animal experimentation – with rather limited contact between the two. Another obvious dilemma is between reduction and refinement where often researchers must choose between trying to cut down on the number of animals used or to limit the amount of discomfort or suffering imposed on the affected animals.

Secondly, we argue that there is a need for a more explicit ethical discussion concerning how to deal with the aforementioned dilemmas. This discussion will both link up with a wider discussion regarding our right to make use of animals to further human goals, and it will relate to specific principles regarding animal use. For example there may be a tension between a principle aiming to minimize the number of animals harmed and a principle of fairness focusing on improving the lot of the animals most badly affected.

Our main conclusion will certainly not be to question the usefulness of the 3Rs principle. Rather it will be a call for a greater awareness of the underlying ethical issues and the need for an explicit discussion of these issues.

II-6-140

A new approach to replacing primates in biomedical science: accessing the views of scientists

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The use of primates in biomedical science has always been a contentious and vehemently debated issue. Yet the arguments on both sides have largely remained unchanged and there has been little progress towards replacing primate models. Presented here is an ongoing PhD project, using a novel multidisciplinary approach, which includes interviewing relevant experts to try to unravel and understand the multifaceted factors involved in the debate. The overall aim is to assess the feasibility of phasing out primate models by investigating two fields of research in particular, schistosomiasis and Parkinson's disease.

The unique insight provided by this approach will be used to discuss how scientists justify their selection of experimental model and choice of research area. Some of the preliminary findings from the interview data will be presented. These will illustrate how factors such as personal ethics, regulation, scientific relevance, and potential health benefits influence how those conducting the studies view the feasibility of replacing primate models in these two fields of research.

II-6-108

Beastly bias and species choice

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Concerns about the welfare of animals are dependent on the assumption that they are sentient, that is, that they have feelings, and those feelings matter to them. Species choice in research is usually determined by scientific reasons, or availability. However, where species choice is possible, European Directive 6106/1/10 requires that animals with the least capacity to experience pain, suffering, distress or lasting harm be used. Within the UK, particular justification is currently required for the use of non-human primates, equids, dogs and cats, and the use of New-World Monkeys over Old-World Monkeys is favoured.

However, species choice on welfare grounds is not a simple matter. Should a fish always be used in preference to a mouse? A mouse to a primate? A bird to a rat? The reality is that it is not easy to determine a species' capacity or relative capacity to suffer. Criteria used to argue for sentience such as encephalisation, complexity and behaviour are not reliable indicators and there is no evidence that pain perception varies. Some argue that primates should be given special status because of their cognitive abilities, but complex behaviours possessed by primates are also found in fish.

Legal controls rightly take account of public views, but these may not always be correct in animal welfare terms. Those making species-choice decisions need to be aware of legislation, but also should make as explicit as possible reasons for considering that one species would suffer more than another in a particular study.

Session II-6: Poster presentations

II-6-497

Endpoints for humane sacrifice in non-clinical safety studies

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The drug development process requires regulatory toxicity studies in animals to assess non-clinical safety aspects. Such studies monitor the potential adverse effects of new drug compounds. It is the ethical responsibility of the scientific community to define the upper acceptable level of adverse effects, while striking a balance between scientific and ethical demands. We established internal guiding principles that describe endpoints for humane sacrifice and assist decision-making when the upper acceptable level of adverse findings is reached. Our guiding principles are based on national and international guidelines and help in the assessment of signs leading to humane sacrifice in experimental animals. The attainment of common guidelines regarding the recognition of animal suffering and appropriate response increases the validity of data from animal studies.

II-6-558

What can regulatory toxicology and other scientific disciplines learn from Three Rs approaches used in the shellfish toxin testing arena?

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European safety monitoring programmes to detect marine biotoxins in shellfish harvested for human consumption have historically relied heavily on the use of Mouse Bioassays (MBAs). MBAs have a number of potentially serious limitations including variability and false negative and positive results. Importantly, in common with many other toxicological assays, shellfish toxin MBAs cause significant animal suffering.

Over the last 15 years, UK laboratories have used a number of strategies for refinement, reduction and finally replacement of these MBAs. Tactics to reduce animal suffering and numbers have included reduction of duration of tests and the number of animals used for each sample, the use of anaesthesia, the use of defined clinical endpoints (rather than death) and alternative pre-screening methods. Using a combination of these approaches, a steady reduction in the use of mice has been achieved, thus significantly reducing animal suffering.

However, such changes have been accompanied by the threat of infraction proceedings for technical non-compliance with European food hygiene legislation. Over-specification in these regulations did not allow for implementation of the Three Rs even where equivalent, or greater, public health protection is afforded by the alternative. A more flexible European Food Safety Regulation was finally delivered in 2010. This required funding (for alternatives research) and prioritisation (for the scientific validation) combined with pressure from enlightened regulators as well as from animal welfare interests.

Can these lessons be usefully applied in other regulatory areas? This presentation will explore the possibilities and consider examples.

II-6-581

The replacement of animals in shellfish biotoxin testing: a global perspective

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Earlier this year, European Union member countries voted to phase out the use of the Mouse Bioassay (MBA) for testing marine biotoxins and replace it, for the majority of biotoxins, with the non-animal LC/MS (Liquid Chromatography-Mass Spectrometry) method. The decision for replacement came after years of pressure from various stakeholders, highlighting the scientific limitations of the lethal test, which causes "substantial" suffering to animals used and displays direct nonconformity with the tenets of EU Directive 86/609 for the protection of animals used for scientific purposes[1]. Nonetheless, there remains much disparity among EU member states in their eagerness to replace the MBA, which currently consumes 600,000 mice[2] in Europe every year, and this becomes even more complex when the situation is observed globally. In a North American context, the use of the MBA is still permitted for testing certain marine biotoxins despite readily available non-animal, scientifically robust methods. The lack of global harmonisation on this issue is problematic when the MBA has been described by the European Food Safety Authority (EFSA) as "inappropriate with inherent uncertainty, variability and poor specificity"[3] for the testing of most biotoxins, and thus cannot be relied upon to ensure safety to consumers. This presentation will articulate a strategy for a harmonised international shellfish- monitoring programme.

1 Article 7: Member states "[....] *shall ensure that a procedure is not carried out if another method or testing strategy for obtaining the result sought, not entailing the use of a live animal".*

2 Intergroup on the Welfare and Conservation of Animals. Report of the 264th Session. Biotoxins and shellfish safety. 8 July 2010.

3 EFSA CONTAM Panel Scientific Opinions, available at: http://www.efsa.europa.eu/en/scdocs.htm