

The **A P C**
Animal Procedures Committee

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Direct Line 020 7035 4776

27th November 2013

Norman Baker MP, Minister of State for Crime Prevention

Dear Mr Baker,

Review of the assessment of cumulative severity and lifetime experience in non-human primates used in neuroscience research

On behalf of my colleagues, I am pleased to bring our final report to your attention. This has been a major, innovative piece of work undertaken by the (past) Animal Procedures Committee's Primate Subcommittee Working Group supported by inspectors from the Animals in Science Regulation Unit. It is the first comprehensive review to be published, in the UK or worldwide, of the potential effects of cumulative severity in complex long term experiments in monkeys.

Traditionally, the classification of severity adopted when applications to undertake animal research were reviewed has been based on the overall severity of one or more procedures. Nevertheless, it is recognized that the potential lifetime experience of an animal should also be considered. This aspect has been particularly emphasised in Directive 2010/63/EU on the protection of animals used for scientific purposes. However, there has been difficulty in providing a coherent set of evidence-based guidelines for assessing this cumulative effect.

In March 2011, the APC established a Cumulative Severity Working Group to review the cumulative effect of long term scientific procedures on the animals involved. The review particularly considered how cumulative severity may be assessed in neuroscience research in non-human primates (macaque and marmoset monkeys) and was asked to consider the following:

- the criteria by which to assess cumulative severity in non-human primates;
- the latest research into understanding the cumulative severity experienced by animals undergoing commonly used procedures, including physiological and behavioural studies;
- the implications of considering cumulative severity for future project licence applications and implications of retrospective reporting under Directive 2010/63/EU; and
- the ethical considerations surrounding cumulative severity.

We called for evidence from a wide range of specialists, practitioners and academics involved with animal scientific procedures. The Working Group visited a number of scientific establishments and actively engaged with animal welfare and protection organisations. A web-based questionnaire was created to establish a common methodological framework for measuring the lifetime experience of the animal. There has been wide engagement and, for the first time, real data have been acquired – some 13,000 data points excluding comments.

The review concludes that little evidence was found (in the majority of non-human primates)

to suggest that, after applying all refinement techniques, the cumulative impact on the animal warrants an increased severity assessment (from a licensing point of view) over that for single events/procedures alone.

The review provides a framework of definitions and scenarios to structure future objective and quantifiable assessments.

The review has identified issues specific to the concepts of cumulative severity and lifetime experience that should be subject to further and future debate:

- the quality of life of primates bred specifically for neuroscience research;
- the conflict between using a small number of subjects for longer or more subjects for a shorter period; and
- the weighting of the impact of the terminal phase against the overall lifetime experience of the animal when assigning severity categories.

The review suggests:

- the wider sharing of best practice in selection of animals, husbandry and in techniques of anaesthesia, surgery, training and post-mortem examination;
- the further development of a multidisciplinary team approach to welfare, in concert with the Animal Welfare and Ethical Review Body, to assess the severity experienced by individual animals, avert the progression of suffering and achieve a timely consensus over decisions about the need to terminate experiments;
- the involvement of all investigators and staff caring for the monkeys in seeking new ways to improve their welfare; and
- the inclusion in publications of the information detailed in the Animal Research: Reporting In Vivo Experiments (ARRIVE) guidelines of the NC3Rs.

The review suggests that further research is required to improve objective methods to assess and quantify:

- pain and distress in non-human primates;
- whether non-human primates experience long-term negative emotional states (akin to anxiety and depression in humans);
- the impact of successive procedures;
- sensitive and robust surrogate biomarkers of cumulative suffering; and
- retrospective assessment based on the continuous, standardised collection of data as the experiment progresses.

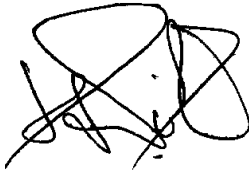
The review also suggests that the Animals in Science Regulation Unit (ASRU) should consider further defining the criteria for designating categories of severity where cumulative experience may be relevant.

A summary of the review's recommendations can be found on pages 9 -14 of the executive summary. The Working Group hopes that this review will inform the debate on the welfare of animals within science and contribute to the future development of regulatory policies based on a more informed understanding of an animal's lifetime experience. The Review was enabled by cooperation between many of those engaged with the welfare of monkeys used in research. The welfare of the monkeys, scientific rigour and public engagement will all be served by building on the trust created. All concerned with this research must continue to work together in a spirit of openness and trust, with the emphasis on mutual education and development through listening and constructive exchange of information (Concordat on Openness on Animal Research, 2012).

In concluding, I would like to bring to your attention the unwavering dedication of the members of the Working Group, not least because of the significant demand on their time (beyond that of their day jobs) which they gave so freely. I would emphasize how much the Working Group appreciated the willingness of individuals and organisations to contribute to this review. I would add my personal thanks to the inspectors in the Animals in Science Regulation Unit who supported the Working Group, and to the Home Office Science Secretariat for their unfailing support.

On behalf of the Cumulative Severity Working Group, I commend to you this review and its recommendations which will be launched on Thursday November 28th 2013 and published on the gov.uk website. Hopefully, the review will be helpful to Dr John Landers (Chair) and the new Animals in Science Committee in taking forward the issues surrounding lifetime experience, classification of severity, retrospective reporting and the 3Rs.

Yours sincerely,

A handwritten signature in black ink, appearing to be 'John Pickard', written over a faint circular stamp or watermark.

Professor John Pickard.