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Animals Scientific Procedures Division
Home Office
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Dear Sir / Madam

Re. Home Office consultation on options for the transposition of European Directive 2010/63/EU on the protection of animals used for scientific purposes

Introduction

1 I am writing on behalf of the Nuffield Council on Bioethics, an independent body that examines and reports on ethical issues in biology and medicine. This response is based on the findings of a two-year inquiry carried out by the Council from 2003 to 2005. The inquiry was led by an expert working party, chaired by Baroness Perry of Southwark and comprised of academic and industry scientists, philosophers, members of animal protection groups, and a lawyer. To inform their discussions, the working party sought advice from a wide range of stakeholders and held a public consultation.[1] Their findings were published in the report, *The ethics of research involving animals,*[2] in May 2005, which included a number of recommendations for policy and practice. A list of working party members and the full method of working can be found in the report.

[1] The responses to the consultation are available to download from the Council's website (where permission was given by the respondent): http://www.nuffieldbioethics.org/animal-research/animal-research-animal-research-consultation-responses

[2] Nuffield Council on Bioethics (2005) *The ethics of research involving animals.* Available at: www.nuffieldbioethics.org/animal-research

2 Despite the widely differing views that existed on the working party, members were able to produce a 'consensus statement', agreeing, for example, that a world in which the benefits of research could be achieved without causing suffering or death to animals was the ultimate goal (paragraphs 15.3-15.20). The report set out a number of conclusions, including that improving the quality of the debate and promoting the 3R's (Refinement, Reduction, and Replacement of animal research) were crucial to reducing disagreement on animal research.

3 We believe that many of the report's recommendations are still relevant today. In this response, relevant paragraphs from the report are set out under the consultation questions they relate to. These do not necessarily answer the specific questions but they do set out additional issues that respondents were asked to cover. Paragraph numbers in the response refer to paragraph numbers in the Council's report.

General comments on the consultation paper

4 The UK has the most detailed legislative framework for animal research in the world, through the provisions of the Animals (Scientific Procedures) Act 1986 (ASPA). **We support Option 3 of the Impact Assessment** to: 'Retain current higher UK standards and requirements' because, following on from the conclusions of our report, the UK standards promote more strongly the 3Rs, and because public trust in the regulation of animal research is likely to be lost if the UK's more stringent measures are relaxed in any way.

5 Despite the UK's high standards, it became clear during the discussions of the working party, and also from responses to our consultation, that views differ on whether the provisions of the ASPA are sufficient in scope and detail; whether they are always interpreted correctly; and whether, in its practical application, the legal requirements are always implemented effectively (paragraph 13.54). The transposition of European Directive 2010/63/EU into UK legislation is therefore a welcome opportunity to consider how the legal protection of animals used in scientific procedures can be improved and how it can be used to further promote the 3Rs in UK research.

6 It should be noted that proper attention to the welfare of animals involved in research and the accountability of scientists who conduct research on animals cannot be achieved merely by having detailed regulations. Regulation can act as an emotional screen between the researcher and an animal, possibly encouraging researchers to believe that simply to conform to regulations is to act in a moral way. It is therefore crucial to promote best practice more actively and to improve the culture of care in establishments licensed to conduct experiments on animals, in addition to imposing strict regulations (paragraph 15.15).

SPECIFIC CONSULTATION QUESTIONS

Article 4: Principle of replacement, reduction and refinement

Question: We propose to transpose the requirements of Article 4 as they stand. Are there any further issues relating to replacement, reduction and refinement we should consider?

7 We support the general requirements of Articles 4. It is crucial that the Three Rs are, and continue to be, enshrined in UK regulation on research involving animals. The principle that animals may only be used for research if there is no other way of obtaining the results anticipated from an experiment is also fundamental.

8 Since its establishment in 2005, the UK's National Centre for the 3Rs has made significant progress in promoting the 3Rs in UK research by, for example, working with funders to review the way the 3Rs are implemented, monitoring the welfare of genetically altered mice, and funding research on 3Rs techniques. Other organisations, such as the RSPCA and the Laboratory Animal Science Association, have also been active in this area. However, there are still areas where more could be done and we outline below the relevant recommendations from our 2005 report that are still outstanding.

Article 47: Alternative approaches

Question: Are there any further issues we should consider in relation to the provisions for alternative approaches set out in Article 47?

9 We observe that for moral justification of animal research it is insufficient to consider only those alternatives which are practicably available at the time of assessing a licence application. The question of why alternatives are not available and what is required to make them available must also be asked. The potential of the Three Rs is far from being exhausted. The Council therefore concluded that there is a moral imperative to develop as a priority scientifically rigorous and validated alternative methods for those areas in which Replacements do not currently exist. It is equally important to devise mechanisms that help in the practical implementation of available validated methods (paragraph 15.12).

Tradition and conservatism

10 Difficulties in relation to implementing Replacements are sometimes cited to dismiss further consideration of the concept as unfeasible, regardless of the exact objectives of a particular research project. Some of those opposed to research involving animals also claim that a far wider range of research than is commonly assumed could be replaced by alternative non-animal methods, if there was sufficient will to do so (paragraph 11.3).

11 If researchers have always used animals and are working in a field that has historically relied substantially on animal research, a change in methodology may not be straightforward, as it is common for scientists to frame research objectives in light of the means available. The creation of opportunities for appropriate lateral thinking is likely to require more than 'better training', and **it may be useful to explore ways of achieving structural and institutional change which allow researchers to reconsider ways in which specific**

research questions can be answered by non-animal methods. This approach could be especially relevant to research fields such as experimental physiology and experimental biology, which have always depended very substantially on the use of whole, living animals and where the only alternative may be not to do the experiment (paragraph 11.30).The new animal welfare body required by the Directive may have an important role in this.

Analysis of the scientific barriers to Replacement

12 In order to make further progress in the development and the implementation of Replacements, and in order to address the range of associated expectations, **it would be desirable to undertake a thorough analysis of the scientific barriers to Replacement and how they might be overcome.** This task cannot be addressed in general terms, but requires an in-depth analysis of specific projects in particular areas of research. Since the unavailability of non-animal methods plays a central role in the cost-benefit assessment carried out under the ASPA, we recommend that Ministers request that the new National Committee for the Protection of Animals used for Scientific Purposes, which will replace the Animals Procedures Committee, undertakes or commissions such an analysis for a series of projects with a wide range of scientific objectives. A clear exposition of obstacles, and strategies for overcoming them would, first, allow research efforts to be focused on problems that must be overcome if animals are to be replaced for a particular purpose. Secondly, such an analysis would identify publicly the scientific problems which are thought to be insurmountable (paragraph 15.62). A promising development is the Replacement programme of the National Centre for the 3Rs, which has explored opportunities for replacing animals in research on nausea and emesis, for example.[3]

Taking account of the international context

13 When considering the replacement of specific types of research by alternative methods, it is important to take account of the international context in which research involving animals takes place. **We therefore welcome the provision in Article 47 which holds that the Commission should take appropriate action with a view to obtaining the international acceptance of alternative approaches validated in the European Union.** Many chemical and pharmaceutical compounds that have been developed are being marketed in countries or regions that have different regulatory frameworks for animal research and testing. There is a range of alternatives that have been internationally accepted for safety testing. Nonetheless, many Replacements are not universally accepted, and the process of validation is lengthy. These processes need to be optimised and initiatives aimed at abandoning and replacing specific types of animal testing at national levels complemented by initiatives at the international level. This is not to say that initiatives in the UK can only be taken once there is consensus at an international level. In the past, the UK has been a leader in working towards change in international policies related to research involving animals. This leadership should be encouraged (paragraph 15.15), for example in the context of the new Union Reference Laboratory which will be established under the Directive.

[3] National Centre for the 3Rs. Replacing animal use. See www.nc3rs.org.uk/page.asp?id=885

Targets for the reduction of animal research

14 One way of motivating and monitoring any proposed reduction of animal experiments would be to set targets. We welcome the concept of targets as a useful and universally used means of measuring progress towards specific aims. But we also see problems in applying such a strategy to research involving animals, where, in many cases, the setting of specific quantitative (numerical) targets is felt by researchers using animals to be unhelpful. Instead, we suggest that reduction could be encouraged and monitored by means of a more flexible approach.

15 One way would be to consider qualitative 'markers of reduction', for example, aimed at reducing research that causes substantial suffering. We recommend that the Government's Interdepartmental Group on the Three Rs should undertake or commission a feasibility study to identify which kinds of reduction markers could be set in particular areas of applied and/or basic research.

16 In principle, reduction markers should only be set if they can be linked to a realistic strategy for developing the necessary Replacement methods that will not compromise the amount and quality of basic and applied biomedical research and testing that would otherwise be licensed by the Home Office. Reduction markers that 'ration discovery' are not compatible with the scientific approach. The development of any strategy should primarily be the responsibility of legislative bodies and governments, as should the task of providing the infrastructure and some of the funding to facilitate the process, in close consultation with stakeholders from academia, industry and animal protection groups. In implementing reduction markers it is crucial that initiatives at the national level are complemented, although not limited by, initiatives at the international level (paragraphs 15.64-15.76).

Article 38: Project evaluation

Question: We propose to transpose the provisions of Article 36, 37 and 38 as they stand. What type of information should be placed in the public domain about the project evaluation process to ensure transparency of the process? Under what circumstances would you expect project applications to be referred to external experts and/or the new national committee required under Article 49? Are there any further issues we should consider relating to project authorisation and evaluation?

17 The cost-benefit assessment is at the heart of the regulation of research on animals in the UK. However, it would be wrong to perceive acting morally simply as following rules. Instead, active and continued scrutiny of the costs and benefits is required from all those involved, before, during and after research. This responsibility cannot be devolved to regulators, and, as the Animal Procedures Committee has emphasised, the system is not intended to function in this way.

18 **We recommend that those involved in reviewing research proposals at every stage prior to submission to the Home Office consider not only the scientific aspects, but also animal welfare in appropriate detail.** Good science and good animal welfare are closely interrelated, and it would be wrong for the scientific review process to ignore animal welfare issues. We are aware that many funding bodies recognise this fact. In addition to assessments by internal review boards, some, such as the Wellcome Trust

and the Medical Research Council, routinely invite external reviewers to comment on welfare issues and the way the Three Rs are considered in research proposals involving the use of animals. However, there is anecdotal evidence that this practice is not universal, and we recommend that other funding bodies review their approach (paragraphs 15.54-15.56).

Article 26 and Article 27: Animal Welfare Body and Tasks of the Animal Welfare Body

Questions: Is there a case for animal welfare bodies to have more extensive membership and functions than the minimum requirement set out in Articles 26 and 27? If so, what additional members and functions should be required or recommended in guidance? Might animal welfare bodies play a role in advising on training and competence? How might 'small' establishments be defined and how might they meet the requirements for animal welfare bodies 'by other means'?

19 Our report highlighted the critical importance of the Ethical Review Process (ERP) and our recommendations on the ERP are relevant to the new animal welfare body required by the Directive.

20 **We concluded that the ERP has the potential to make a greater contribution to the identification, promotion and implementation of the Three Rs and could play a more proactive role in identifying best practice and helping to facilitate exchange of information.** When the ERP was established in 1999, one of its main objectives was to promote the application of the Three Rs. However, in practice, many ERPs focus on the review of licence applications, and although this includes consideration of the Three Rs in relation to the specific project, there is potential for a more general contribution. For example, some ERPs have dedicated Three Rs groups that review husbandry and procedural issues. We acknowledge that some organisations, particularly the LASA and the RSPCA, have organised meetings for ERP members in the past to assist this process. We support this approach and recommend that these two organisations, together with other stakeholders where appropriate, identify a systematic and sustainable strategy to ensure that the ERP contributes most effectively to developing best practice in the Three Rs (paragraph 15.60).

Article 46: Avoidance of duplication of procedures

Question: We propose to transpose the provisions of Article 46 as they stand. Are there any further issues we should consider relating to avoidance of duplication of procedures?

21 In our inquiry, we could not explore the question of the extent to which duplication occurs, or the feasibility of devising mechanisms that help to avoid the duplication of research. But we are clear that, in principle, **duplication is unacceptable and we welcomed the approach underlying the UK Government's Inter-Departmental Data Sharing Concordat.** The Animal Procedures Committee also welcomed the Concordat in 2003 but was concerned about the voluntary nature of the Concordat, and considered whether more binding measures, such as legislation, will be needed to achieve the Concordat's aims.

22 Implementation of Article 46 may lead to renewed scrutiny of the effectiveness and openness of data sharing policies, which we welcome. In 2005 we recommended that **Ministers should consider conducting a systematic study on specific issues raised by the possible duplication of research,** and it may be timely to conduct such a review now. It would be useful to assess the extent of the problem and, where appropriate, identify strategies for the avoidance of duplication nationally and internationally. Consideration could also be given to the question of whether duplication occurs because some kinds of data are not made publicly available when experiments fail. It would be especially undesirable if researchers wasted time and effort in duplicating experiments that have elsewhere been found to be unsuccessful. The study could also consider whether funding bodies would have a role in sharing or making available information about past or current research, in order to avoid duplication (paragraph 15.68-15.70).

Article 15 and Annex VIII: Classification of severity of procedures; Article 39: Retrospective assessment; and Article 54: Reporting

Questions: Are there any areas in which the Annex VIII severity classification is unclear? Are there any additional examples of severity that might be included in guidance on the application of the proposed severity classification system?

Question: Should the UK continue to publish a full range of statistics as in the current annual statistics report? Is there scope for streamlining UK statistics? Are there additional statistics it would be useful to publish?

Question: Should we extend the requirement for retrospective assessment to some or all projects involving procedures classified as "mild" or "non-recovery"? What should be the process for retrospective review and should this involve the animal welfare body?

23 The Annual Statistics of Scientific Procedures on Animals, published by the Home Office, have an important role in providing information about animal experimentation. At the same time, there is wide agreement that the data are presented in ways that are not readily accessible to lay people, and that the presentation could be improved. In particular, the Statistics have been criticised for not providing clear answers to the following questions: (i) what is the nature, level and duration of pain, suffering and distress actually experienced by animals used in the different kinds of procedures? and (ii) how many animals are used in procedures and related activities?

24 Information about the degree of pain and suffering can, in some sense, be inferred from the Statistics about the severity bands assigned to granted project licences (*mild, moderate* or *substantial).* But over the five-year period of a project licence, a range of different protocols, themselves assigned different severity limits, may be carried out. It is questionable how meaningful it is to average out the different limits under one band, in order to provide the public with accurate information. For example, it may be the case that a project that contains ten mild protocols, each involving 10,000 animals, and one protocol with a substantial severity limit involving 50 animals, would still be classified as mild (paragraph 15.25-15.27).

25 Information about the suffering that animals involved in procedures experience in practice is unsatisfactory. **We recommend that the Home Office should make retrospective information about the level of suffering involved during procedures publicly available.** In gathering this information

the Home Office should also obtain and make available, retrospectively, information about the extent to which the scientific objectives set out in applications have been achieved (paragraph 15.28). Therefore, in response to the consultation question above, we urge the Home Office to go beyond the Directive and extend the requirement for retrospective assessment to some or all projects involving procedures classified by the Directive as 'mild' or 'non-recovery'.

26 In terms of communication of severity to the public, **we recommend that the current system of severity banding for project licences and the severity limits for procedures should be reviewed, particularly the use of the *moderate* category** which covers a wide range of different implications for animal welfare. For the general public, the category *unclassified*, which refers to protocols and procedures involving terminally anaesthetised animals, is too vague to be informative, and should be clarified (paragraph 15.30). **We also recommend that the annual Statistics should provide case studies of projects and procedures that were categorised using the severity bands.** These case studies should also include examples of animals used over extended periods of time and should describe not only their immediate involvement in research but also the range of factors that influenced their life experiences, such as the conditions of breeding, housing and handling (paragraph 15.29).

27 The Statistics give details about the total number of *animals* used for the first time in a year, and the total number of *procedures* initiated in that year. As we have said, the term procedure refers to a wide range of activities, with very different implications for animal welfare which may arise from breeding, the withdrawal of blood, or experiments where death can be the endpoint. It is not straightforward to infer from the number of procedures undertaken how many animals have experienced what kind of pain, suffering or distress (paragraph 15.31).

28 The humane killing of animals by means set out in Schedule 1 of the ASPA, for whatever purpose, is not itself a licensed procedure. Animals killed in this way are therefore not recorded in the Statistics. Many would argue that possession of a life is a morally relevant feature, and that it is therefore important to provide information about the number of animals that are killed humanely. We realise that the system of collecting data about the numbers of animals used in research is very complex and that care needs to be taken to avoid making existing administrative processes more onerous. Nevertheless, we think it highly desirable to present clearer information about how many animals of a particular species experience pain, suffering and distress, to what degree, and for how long. **We therefore recommend that the Statistics be revised to provide this information, including details about the number of animals killed under ASPA Schedule 1** (paragraph 15.33).

Please do not hesitate to contact me if you would like to discuss any of these points further. Full details of the Council's report and recommendations are available through the Council's website at: www.nuffieldbioethics.org/animal-research

Yours sincerely

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