

## **ESF-EMRC Position on the Proposed Revision of the Directive on the Protection of Animals Used for Experimental and Other Scientific Purposes (86/609/EEC)**

**The aim of this paper of the European Medical Research Councils (EMRC), the Standing Committee for Medical Sciences at the European Science Foundation (ESF), is to provide an input into the discussions on the revision of the EC Directive 86/609/EEC on the protection of animals used for experimental and other scientific purposes.**

**This paper summarises the current scientific and technical positions on four elements of the proposed revision of the Directive of those medical research councils in Europe that are ESF Member Organisations (MOs). It builds on previous work of the ESF<sup>1</sup> and draws on documents produced by ESF MOs at the various stages of the consultation process for the revision of this Directive.**

**One of the key reference documents for this paper is a non-public version of the draft revised Directive, which was circulated to stakeholders, including ESF MOs, during the consultation phase with the European Commission's Directorate General Environment.**

### **Introduction**

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The current Directive 86/609/EEC on the protection of animals used for experimental and other scientific purposes was published by the European Commission (EC) in November 1986<sup>2</sup>. It was adopted more than 20 years ago and is currently being revised by the European Commission's Directorate General Environment.

In the light of new scientific developments and advances in the understanding of animal welfare, and given the enlargement of the European Union (from 12 to 27 member states) since the first publication of this Directive, a revision is strongly supported and welcomed by the ESF-EMRC Member Organisations (MOs).

A revised Directive should respect the welfare of animals while guaranteeing the health and well-being of all Europeans. Ethical considerations and animal welfare must be an integral part of the ethos of all establishments that use animals for scientific purposes. In the specific case of biomedical research, the revision of the Directive, particularly with reference to non-human primates, should be evidence-based and ensure that the balance between research needs and animal welfare is maintained and that the important continuation of necessary work requiring animals is not jeopardised<sup>3</sup>.

### **Administrative burden and triple licensing scheme**

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The draft revised Directive proposes more stringent measures on the use of animals in experiments, with the imposition of triple authorisation by the competent authority of persons (*Article 20*), establishments (*Article 21.1*), and projects (*Article 35*) which is currently the case in most countries and has proved to be very effective in reducing the number of animals used in procedures.

However, in addition, the Directive proposes that administrative authorisation of projects should be submitted to a comprehensive ethical review system, such that each establishment for the breeding, supplying or use of animals shall be required to have a permanent ethical review body (*Article 25*). This should take into consideration the fact that several EU Member States, including France, Germany, Italy and the United Kingdom already have their own procedures for approving experiments on animals and thus care should be taken that there is no unnecessary duplication. Furthermore, establishing a legal requirement for an additional mechanism for a separate ethical review does not seem to be neces-

sary and, instead, a consistent provision for the ethical evaluation should be found, in order that the approval process is conducted in the most cost-effective and timely means possible without quality reduction<sup>4</sup>. By placing a significantly increased administrative burden on institutions using animals for research, important resources will be consumed, which could incur the risk of discouraging biomedical research.

## Use and breeding of non-human primates (including great apes)

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### i) Banning the use of great apes and other non-human primates

It is proposed to ban the use of great apes in experimentation, except in research used for the preservation of the species (*Article 7.2*). While acknowledging that there is some public support for such a ban and that the European Parliament adopted a written declaration of support in June 2007<sup>5</sup> for the ending of the use of apes in scientific experiments, a complete ban would not be advisable. It is important to consider that virtually no great ape is used in Europe for experimentation, except in Germany and Belgium for minimally invasive cognitive research, and that Austria, The Netherlands, Spain, Sweden and the United Kingdom have either total or *de facto* bans in place to prohibit their use<sup>6</sup>. However, it is not possible to predict future health crises for which their immediate use may be necessary. The only current models for research on hepatitis C, for example, are based on the chimpanzee<sup>6</sup>.

On the broader issue of banning all non-human primates in scientific experiments, a preliminary analysis by the Inserm National Working Group<sup>7</sup> on peer-reviewed journals with the terms ‘monkeys’ or ‘non-human primates’ indicates that this would result in a significant reduction in the amount of biomedical research undertaken in Europe, particularly in neurosciences and zoology.

This is supported by a recent joint statement of the German Research Foundation (DFG) and the Max-Planck Society in which they state ‘*non-human primates are particularly useful in legally mandated drug testing, for the development of vaccines, to study neurophysiological questions, and in infection-related and behavioural biology*’<sup>8</sup>. In Europe, China, Japan and the USA, reports have shown that the use of non-human primates in biomedical research is absolutely necessary. The Weatherall Report on The Use of Non-Human Primates in Research concluded that ‘*there is a strong scientific case for maintaining work on non-human primates for carefully selected research problems in many of the areas studied, at least for the foreseeable future*’<sup>9</sup>. Another report from the US National Academy of Sciences stated that ‘*non-human primate resources must be in place if the biomedical community is to respond appropriately to any threats or challenges to the Nation’s health*’<sup>10</sup>.

### ii) Breeding of non-human primates

In the draft revised Directive, it is proposed to use non-human primates only of the second breeding generation or later in scientific experimentation (*Article 9.1*), which would have the effect of prohibiting the use of these primates in Europe and doubling the number of animals in captivity over the course of 10 years<sup>4,11</sup>. This is because nearly all of the primates used in the EU come from colonies that are artificially bred and are mainly of the F1 generation (i.e. first generation born in captivity). The ESF-EMRC MOs support this article but would like to include a timeline in the Directive of approximately 10 years, during which time, the infrastructure and research in Europe can work towards the implementation of this article. Immediate reinforcement of this article would have implications for the existing infrastructure for housing primates across Europe and hamper or delay important research. Finally, it is unclear who will bear the costs of developing the proposed infrastructure.

## Technical procedures

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Chapter III of the draft revised Directive addresses the procedures used and a number of concerns must be raised here. *Article 14.1* specifically deals with the issue of stress levels. The plan is to introduce three categories, which are not yet specified. In addition to intensity, the duration and frequency of the stress are to be considered, together with deprivation of ethological needs and frequency of intervention. This would create considerable problems for neurophysiological research involving primates if the classification of the stress levels is not carefully defined. It has to be taken into account in all cases that animals must have a chance to adapt to a general situation, which is then considered less stressful<sup>12</sup>.

Where long-term stress experiments have been shown to be necessary, *Article 14.2*, which proposes a ban on long-term stress experiments, could restrict the modelling of chronic diseases for the benefit of patients and neurophysiological research.

## Alternatives to animal testing and the 3Rs

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The draft revised Directive ensures that the principle of the 3Rs (reduction, replacement and refinement) – notably absent from the current Directive – is rigorously applied. *Article 45* states that ‘*The Commission and Member States shall contribute to the development and validation of alternative approaches which could provide the same level of information as that obtained in procedures using animals but which do not involve the use of animals or use fewer animals or which entail less painful procedures, and shall take such other steps as they consider appropriate to encourage research in this field*’.

It is important for the welfare of animals and for the maintenance of public trust that there is continued and increased funding for research aimed at alternatives (3Rs)

for animals in research. Alternative methods should replace animal experiments on the basis of an examination of scientific work, published in peer-reviewed journals<sup>7</sup>. The scientific community takes seriously its responsibility to implement the most up-to-date knowledge on the 3Rs in their experiments. If a revision of the Directive is to result in stronger constraints on the use of animals, this will not necessarily encourage the development of alternative methods, which are currently limited, particularly in the field of research activities on human health threats. The comment in the working mandate of the EC's Scientific Committee on Health and Environmental Risks (SCHER) supports this in stating '*not enough alternative methods are yet available to replace the use of non-human primates in all areas of biomedical research today*'<sup>13</sup>.

Article 46, states '*Each Member State shall, within, one year after entry into force of this Directive, designate a national reference laboratory for the validation of alternative methods replacing, reducing and refining the use of animals*'. The ESF-EMRC MOs do not support this article, as it should not be necessary to have a national reference laboratory in each EU Member State for the validation of alternative methods; different countries could collaborate and share research data.

## Summary and recommendations

Welcoming the proposal to revise the Directive 86/609/EEC, ESF-EMRC MOs would like to express their concern that if the Directive is implemented in its current form, it will significantly hinder medical research in Europe to the detriment of European patients, particularly in the area of understanding chronic neurological diseases such as Parkinson's disease and treating other conditions such as spinal cord injuries. It is essential that there is a more comprehensive consideration of the needs of science and its impact on society in the revision of the Directive, with specific emphasis on the following points:

- Ensure that the triple authorisation and ethical review systems do not create an unreasonable administrative burden, use excessive resources or result in unnecessary duplication of existing national requirements;
- Reconsider both the proposed ban on the use of great apes, with the insertion of a clause on their use in exceptional health crises, include a timeline in the provision that non-human primates only of the second generation are used; and propose reasonable financial provisions to help in the development of this infrastructure;
- Introduce a stress factor catalogue that meets scientific, not emotional criteria, to be listed as an Annex when the Directive takes effect. The absence of such a document may result in grave problems arising not only from research involving primates but for the classification of long-term stressful experiments. Reconsider the ban on long-term stressful experiments as it could eliminate the modelling of chronic diseases;

- Stimulate 3Rs research and encourage and support alternative methods to animal testing. These methods should be used following the gold standard of scientific evaluation (publication in peer-reviewed journals) and validation (European Centre for the Validation of Alternative Methods, ECVAM). The scientific community also has a responsibility, with the help of ECVAM, to keep itself up to date with these methods. The ESF-ERMC MOs do not support the proposal that each EU Member State should designate a national reference laboratory for the validation of alternative methods replacing, reducing and refining the use of animals but instead believe that collaboration and sharing of data on this topic should be encouraged across Europe.

## References

1. Use of Animals in Research. ESF Science Policy Briefing (SPB) 1<sup>st</sup> ed., September 2000 (SPB 9); 2<sup>nd</sup> ed., August 2001 (SPB 15). [www.esf.org/research-areas/medical-sciences/publications.html](http://www.esf.org/research-areas/medical-sciences/publications.html)
2. Council Directive 86/609/EEC of 24 November 1986 on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31986L0609:EN:HTML>
3. Letter from Sir Leszek Borysiewicz, Head of the Medical Research Council, (UK) to Commissioner Potočník, 19 February 2008
4. Letter from Professor Peter Gruss, President of the Max Planck Society, (DE) to Commissioner Potočník, 26 November 2007
5. European Parliament Written Declaration 0040/2007 On Non-Human Primates in Scientific Experiments, April 2007 [http://ec.europa.eu/environment/chemicals/lab\\_animals/pdf/declaration\\_nhp\\_en.pdf](http://ec.europa.eu/environment/chemicals/lab_animals/pdf/declaration_nhp_en.pdf)
6. Minutes of the CLORA (Association for French Research Organisations) Meeting on 'Animal Testing', 17 April 2008
7. Comments of the Inserm Working Group in response to a public consultation (deadline 6 June 2008) on the working mandate proposed by the EC-Directorate General Health and Consumer Affairs (SANCO) for the Scientific Committee on Health and Environmental Risks (SCHER) on the need for non-human primates in biomedical research, production and testing of products and devices [http://ec.europa.eu/health/ph\\_risk/committees/04\\_scher/scher\\_call\\_info\\_03\\_en.htm](http://ec.europa.eu/health/ph_risk/committees/04_scher/scher_call_info_03_en.htm)
8. Joint Statement of the German Research Foundation (DFG) Senate Commission on Animal Protection and Experimentation and the Commission for Issues on Animal Welfare of the Max-Planck Society (MPG) for Questions on the Use of Non-Human Primates in Research, May 2008
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10. Demand for Rhesus Monkeys in Biomedical Research: A Workshop Report, Washington DC, April 2002. [http://dels.nas.edu/ilar\\_n/ilarjournal/44\\_3/v44n03workshop.pdf](http://dels.nas.edu/ilar_n/ilarjournal/44_3/v44n03workshop.pdf)
11. Observations by Dr François Lachapelle and colleagues, Inserm, 16 May 2008
12. Comments from the German Research Foundation (DFG) Senate Commission on Animal Protection and Experimentation on the draft Directive from discussions in March 2008 and e-mail communication with the Max-Planck Society
13. Working Mandate of the Scientific Committee on Health and Environmental Risks (SCHER) as described in Reference 7 above [http://ec.europa.eu/health/ph\\_risk/committees/04\\_scher/docs/scher\\_q\\_073.pdf](http://ec.europa.eu/health/ph_risk/committees/04_scher/docs/scher_q_073.pdf)

# ESF-EMRC MOs Consulted

## Austria

- Fonds zur Förderung der wissenschaftlichen Forschung in Österreich (FWF)  
*Austrian Science Research Fund*
- Österreichische Akademie der Wissenschaft (ÖAW)  
*Austrian Academy of Sciences*

## Belgium

- Fonds National de la Recherche Scientifique (FNRS)  
*National Fund for Scientific Research*
- Fonds voor Wetenschappelijk Onderzoek-Vlaanderen (FWO)  
*Research Foundation Flanders*

## Bulgaria

- Българска академия на науките (BAS)  
*Bulgarian Academy of Sciences*

## Croatia

- Hrvatska akademija znanosti i umjetnosti (HAZU)  
*Croatian Academy of Sciences and Art*

## Cyprus

- Ίδρυμα Προώθησης Έρευνας (RPF)  
*Cyprus Research Promotion Foundation*

## Czech Republic

- Akademie věd České republiky (ASCR)  
*Academy of Sciences of the Czech Republic*

## Denmark

- Forskningsrådet for Sundhet og Sygdom (FSS)  
*Danish Medical Research Council*

## Estonia

- Eesti Teaduste Akadeemia  
*Estonian Academy of Sciences*
- Eesti Teadusfond (ETF)  
*Estonian Science Foundation*

## Finland

- Suomen Akatemia/Finlands Akademi  
*Academy of Finland*

## France

- Centre National de la Recherche Scientifique (CNRS)  
*National Centre for Scientific Research*
- Institut National de la Santé et de la Recherche Médicale (Inserm)  
*National Institute for Health and Medical Research*

## Germany

- Deutsche Forschungsgemeinschaft (DFG)  
*German Research Foundation*
- Max-Planck-Gesellschaft (MPG)  
*Max Planck Society*

## Greece

- ΕΘΝΙΚΟ ΙΔΡΥΜΑ ΕΡΕΥΝΩΝ (NHRF)  
*National Hellenic Research Foundation*

## Hungary

- Magyar Tudományos Akadémia (MTA)  
*Hungarian Academy of Sciences*
- Országos Tudományos Kutatási Alapprogramok (OTKA)  
*Hungarian Scientific Research Fund*

## Iceland

- RANNIS  
*Icelandic Centre for Research*

## Ireland

- Health Research Board

## Italy

- Consiglio Nazionale delle Ricerche (CNR)  
*National Research Council*

## Lithuania

- Lietuvos Valstybinis Mokslo Ir Studijų Fondas  
*Lithuanian State Science and Studies Foundation*

## Luxembourg

- Fonds National de la Recherche (FNR)  
*National Research Fund*

## Netherlands

- Nederlandse organisatie voor wetenschappelijk onderzoek (NWO)  
*Netherlands Organisation for Scientific Research*
- Koninklijke Nederlandse Akademie van Wetenschappen (KNAW)  
*Royal Netherlands Academy of Arts and Sciences*

## Norway

- Norges Forskningsråd  
*The Research Council of Norway*

## Poland

- Polska Akademia Nauk (PAN)  
*Polish Academy of Sciences*

## Portugal

- Fundação para a Ciência e a Tecnologia (FCT)  
*Foundation for Science and Technology*

## Romania

- Consiliul National al Cercetării Stiintifice din Invatamantul Superior (CNCSIS)  
*National University Research Council*

## Slovakia

- Slovenská Akadémia Vied (SAV)  
*Slovak Academy of Sciences*

## Slovenia

- Slovenska Akademija Znanosti in Umetnosti (SAZU)  
*Slovenian Academy of Sciences and Arts*

## Spain

- Consejo Superior de Investigaciones Científicas (CSIC)  
*Council for Scientific Research*
- Comisión Interministerial de Ciencia y Tecnología (CICYT)  
*Interministerial Committee on Science and Technology*

## Sweden

- Vetenskapsrådet (VR)  
*Swedish Research Council*

## Switzerland

- Schweizerischer Nationalfonds (SNF)  
*Swiss National Science Foundation*

## Turkey

- Türkiye Bilimsel ve Teknolojik Araştırma Kurumu (TÜBİTAK)  
*The Scientific and Technological Research Council of Turkey*

## United Kingdom

- Medical Research Council (MRC)

## EMRC Chair:

Professor Liselotte Højgaard, Clinic of Clinical Physiology, Nuclear medicine & PET, University of Copenhagen, Copenhagen, Denmark

## ESF/EMRC Office:

Dr. Carole Moquin-Patthey, Head of Unit  
Dr. Fiona Kernan, Junior Science Officer

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