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CONTACT INFO

**tel** +44 7990 906145

**email** matfield@ebra.org

**postal address**
25 Shaftesbury Avenue
London W1D 7EG
United Kingdom

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# Public Consultation on Revision of Animal Research Directive

**Individual researchers now have a chance to influence the content of the new Directive - and it is importan that they express their views to the European Commission**

The European Commission has recently started the public consultation on their proposals to revise Directive 86/609, which regulates animal experimentation within the EU. The Commission have adopted a careful approach with the consultation, by offering two quite different versions: one for the public and the other for experts in "animal welfare, animal testing, animal science, natural sciences (especially biology, medicine, pharmacology and toxicology), legal and economic affairs related to these areas."

It will be very important for academic researchers to respond to the expert consultation. Some of the things being proposed could have a seriously harmful effect on important areas of research. Although the consultation form is lengthy, it is only necessary to comment on those parts which are of concern. The number of responses received to the consultation will be very important. If only a few hundred responses are received, the European Commission may conclude that such a limited response indicates that few people have concerns about the proposals.

The closing date for submissions, which can only be made via the web (http://ec.europa.eu/environment/chemicals/lab_animals/ia_info_en.htm#5), is 18th August.

The public consultation is fairly short and concentrates on opinions about the appropriate levels of protection for laboratory animals, the acceptability of various purposes for using animals, which species should be used, transparency and alternative methods.

The expert version of the consultation will be very important because it is designed to solicit comments on the preliminary findings of the impact assessment that is being conducted on the proposals for the revision. This means that the questionnaire gives a detailed explanation of the new provisions that are being considered for inclusion in the new Directive. This is the first time the proposals have been set out in such detail. Because many academic researchers have not been consulted by the company preparing the impact assessment, it is particularly important to respond to this consulation to ensure that the views of the scientific community are properly understood before legislation is drafted.

Although there are only about 20 specific proposals, the questionnaire is quite long – the downloadable pdf version is 64 pages long – because it gives background information to each of the proposed measures. Indeed, it is sufficiently complex that the instructions tell users to download the Word version, draft out their responses and cut and paste them into the response web page. This page can only be accessed for 90 minutes before it shuts down, which would probably not be time enough to write all the replies necessary on the page itself.

As expected, it appears that the overall effect of the proposals will be to create a new Directive similar to the United Kingdom's national legislation, considered by many to be the most rigorous of any EU Member State. This will undoubtedly result in a significant increase in administrative burden both for researchers and the national authorities in those member states with more relaxed legislation.

The results of the consultation will be made public, but the expert version of the consultation allows users to withold their name and institution from being made public.

In the following articles in this EBRA Bulletin, we examine the few proposals which are likely to cause serious problems for EU bioscience research, identify the ones that will produce a general increase in administrative burden in certain member states and, finally, identify those proposals which are reasonable and unlikely to cause any problems.

Further information about any of these proposals or their effects, or advice about responding to the consultation, can be obtained from EBRA, by e-mailing matfield@ebra.org.

## Proposal puts primate research at risk

## Incorrect information has resulted in a proposal that could force most promate research out of Europe

The most worrying proposal included in the expert consultation is that only second generation (ie F2) captive-bred primates could be used, although they suggest that there should be a phase-in period for this change.

The 2002 figures show that 9,267 non-human primates were used in scientific procedures in the EU. Of these, 1095 were new-world primates, the vast majority of which would have been marmosets, which are routinely bred in long-term colonies and this would be at least second generation captive bred. The remaining 8075 are old world primates, nearly all of which would be macaques. The vast majority of these are imported into the EU.

This proposal to only permit the use of F2 purpose-bred primates is based upon a serious factual error in the background information, which states, “In 2002, about 60% of the NHPs used for scientific purposes were imported from outside the EU, more than 90% of them being macaques. All these macaques are F2 purpose-bred.” In fact, these animals were, and continue to be, first generation, or F1, purpose-bred. There are no significant numbers of F2 purpose bred macaques imported into the EU.

The main macaque breeders are in Mauritius, Philippines. China and Israel. These breeders take animals captured from the wild and breed them, selling the offspring (the F1 captive bred generation). To create a supply of F2 animals the breeders would either have to substantially reduce their sales of F1 animals so they can breed them or substantially increase the number of animals taken from the wild, neither of which they want to do. There is a high world demand for purpose-bred macaques, particularly from the USA. Since these breeders can sell all the F1 animals they breed to buyers in the USA, they have not shown any particular interest in breeding F2 animals. The size of the EU market for purpose-bred macaques is not large enough to make it likely that the breeders could be persuaded to create an F2 supply.

It is estimated that between 90% and 95% of all macaques used in the EU are imported from outside the EU. This is a higher figure than recorded in the EU statistics on animal experimentation, but that is because some animals are imported by a supplier and then sold on to the final user. In the EU statistics these primates are counted as coming from within the EU, simply because the laboratory buys them from the local supplier, not direct from the overseas breeder.

The vast majority of macaques are used in the EU for the development and testing of pharmaceuticals and vaccines, although a significant minority are used in academic research in the neurosciences. Since there is little prospect of a supply of F2 animals becoming available, this proposal would cause all pharmaceutical and vaccine industry primate work and much academic primate neuroscience research to be moved out of the EU. The immediate effects on these fields of EU research and development would be very serious indeed.

## Openess and transparency - proposals not well designed

**The new Directive wants a high level of transaprency and public information, but the proposal for how to achieve this will be very complex and not achieve the objectives**

The proposals for the revised Directive aim to promote openness and transparency. It is proposed that all non-confidential information from project authorisations and ethical review to be made public, with exceptions for information that would risk intellectual property rights or personal safety.

The legal definition of confidential varies from Member State to Member State and there is no European case law on the subject. However, in many Member States the definition is quite broad and would result in the majority of the content of project authorisations and ethical review material being non-disclosable. Experience with such disclosures suggests that each document has to be reviewed on a line-by-line basis by an expert to identify the material that cannot be disclosed. This creates a substantial administrative burden, significant delays in releasing documents and limited additional transparency as so much of the resulting documentation is deleted that it becomes almost meaningless.

The United Kingdom routinely publishes anonymous, non-technical summaries of all project authorisations, written by the applicants and agreed by the national authority, as part of the authorisation process. This provides significantly greater transparency and public information, whilst safeguarding the identity of the applicant, with minimum additional administrative burden. We consider that a similar system should be incorporated in the revised Directive instead of the present poorly-designed proposal.

## Project authorisation and ethical review

**FThe proposals for project authorisation and ethical reviw systes look good in principle, but duplication of function is likely to cause pointless administration and delays**

authorisation and ethical review. In principle, this seems to be a good idea, but there are some potential problems.

There would be a significant increase in the administrative burden for researchers in those Member States that currently grant authorisations for broad, on-going programmes of research, since it seems highly likely that this proposal refers to such discrete, time-limited projects.

It is proposed that projects should be authorised if they meet three criteria. First, that they meet a set of fairly basic regulatory points, which should not create any real problems. Second, that there should be a deadline by which the regulatory authority must reply to an application. This would be very welcome but, as it is currently worded it could be meaningless. The reply could simply be, “We are considering your application.” This proposal will only be of any value if the deadline is for the authority to approve (or reject) the application.

The third criterion is that the project should have a positive ethical review. Ethical review would be carried out within each establishment, using a set of criteria defined by the new Directive. In principle, this would be sensible. Most countries already have local ethical review bodies. The ones that dont - typically becaue they have regional bodies - will face a noticable administrative burden. Howevr, the main problem is that there is likely to be a significant unnecessary administrative burden and delays to authorisations in many Member States caused by duplication between the authorisation and ethical review systems.

Several Member States currently have project authorisation systems which use some or all of the criteria proposed for the ethical evaluation system. It is unrealistic to expect that regulatory authorities would voluntarily remove criteria from their authorisation systems and rely on local ethical evaluation systems to make these judgements for them. Why do we know that this is unrealistic? Over the last decade, ethical review systems have evolved in most Member States. Duplication of function, with projects being assessed twice, using the same criteria, is already happening in some countries. In the worst case, essentially all the harm-benefit and justification criteria are duplicated, with the two processes operating in sequence, rather than in tandem, wasting time and effort. Unless the proposal includes some measures to prevent this duplication, a requirement to have these criteria in the ethical evaluation system will simply lead to duplication of function and unjustified additional administrative burdens and delays to project authorisations.

## New animal welfare and caging standards

**Higher standards of animal welfare and caging will be mandatory and lead to substantial additional costs**

As expected, it is proposed that compliance with the Council of Europe ETS123 standards of animal caging and welfare should be mandatory. This is inevitable and it will be very expensive. However, it will produce a major increase in laboratory animal welfare across the EU, which is obviously worthwhile.

The EU has signed up to European Convention ETS123 so it is inevitable that these standards will become part of the revised Directive. Currently, the Directive contains non-mandatory guidelines identical to the old ETS123 guidelines. These were quite basic, but were recently revised and updated and many establishments across the EU have started to implement the new ETS123 standards.

Actually, it is unlikely to make much difference whether the ETS123 standards are implemented in the revised Directive as guidelines or made mandatory. In either case, the vast majority of EU establishments will implement them in the next few years. However, this will produce a very significant one-off cost (estimated to be in excess of a €1 billion) and a substantial increase in ongoing costs, to meet the lower stocking densities in the new ETS123 standards.

Making these standards mandatory will mean that all establishments have to implement them sooner than if they were only guidance, but the Directive will specify a phase-in period. Bearing in mind that the new Member States have only recently had to implement the old ETS123 standards and that the academic sector has significant problems finding the funding to meet new capital requirements, the minimum sensible phase-in period should be 5 years, and the ideal period should be 10 years.

## Should $CO_2$ euthanasia be banned?

**A proposal to ban $CO_2$ euthanasia will please some but many experts consider it to be premature**

Carbon dioxide has been used as a routine method of euthanasia for decades, and for some time there has been a debate about how humane the method actually is. It is proposed that the new Directive should ban this form of euthanasia.

However, many experts in laboratory animal science consider that such a move is not justified by the evidence and that further research is needed. A recent study of $CO_2$ euthanasia, to be soon published by the UK National Centre for the Three R's, concludes that it is premature to ban

it as there is no practical alternative that could be said to be more humane.

In addition, it is assumed that the cost of this proposal would simply be the one-off cost of buying the apparatus necessary for an alternative method in every establishment. However, all of the alternative methods of euthanasia require significantly more time and manpower for the same number of animals. This means that the proposal would result in substantially increased costs on a ongoing basis, without any certain animal welfare benefit.

## The rest of the proposals

**There are several other measures proposed for the revised Directive, but we consider that most of them will not cause significant problems for biomedical researchers in the EU**

In total, there are about 20 specific proposals described in the expert consultation about the revision of the Directive and the majority of them would either have no real effect on biomedical research or result in only limited additional costs in certain countries, administrative burden. In this article we present a quick overview of these proposals.

Technically, the use of animal in fundaental research is not controlled by the existing Directive. However, all the Member States (with the excetion of a few of the new ones) have national legislation the regulates all types of animal experimentation, both fundaental and comerical. Accordingly, the proposal that the revised Diretive should regulate fundamental research will have little or no effect in reality.

It is proposed that animals bred to provide fresh tissue for use in research (ie where no scientific procedure is carried out on the living animal) should be regulated by the Directive, unless they are killed by a recognised humane method. once again, thei is likelty to have little or no impact because almost all killing is carried ou by recognised humane methods.

It is also proposed that the use of decapod, cephalopod and cyclostome species should be regulated by the new Directive. There appears to be ahrdly any research on these species in the EU, so this proposal is unlikely to have any significant ipact.

Another proposal is that the foetal and embryonic forms of mammalian species should be regulated after two thirds of the way through gestation. The vast majority of foetal and embryonic fors used in research are either non-mammalian or in circumstances where they are in utero, so that the mother animal is involved and the experiment has to be regulated

anyway. Once again, this proposal is unlikely to have any real impact.

The proposal that the new Directive should cover the use of animals in education and training will have some impact. There is a limited amount of student education involving experimental procedures on animals and some training of scientists and technicians. This will require ethical review and authorisation, resulting a limited additional level of adminsitrative burden. Medical device training courses (eg laproscopic surgery) use a greater number of anials and these will experience a more significant additional burden of costs and administration.

The consultation includes the ides of retrospective reviews of projects to assess the harms to the animals and scientific or other benefits that came out of the project. A harm-benefit assessment would be part of the initial ethical review of each project, so the retrospective review would act as a double-check on this. However, the consultation takes the view that the time and effort required for retrospective review would not justify the benefits. We agree with this.

In addition to ethical review bodies in each establishment, it is proposed that there shouls be a national body to set standards for ethical review. Most Member States already have such a body, or something very similar.

With one small exception, the use of great apes in research has now finished in the EU, so the peoposal for a ban on their use, with only very limited exceptions, simply reflects the current situation.

The proposal that all establishments should be inspected twice each year, with one of the inspections unannounced will cause a significant additional cost and administrative burden in the majority of Member States, where inspection is less frequent. However, inspection is a good way of ensuring compliance with the regulations and will increase public confidence that laboratory animals are properly treated. Moreover, it is politically impossible to argue against such a proposal without looking as if one wants to get away with poor compliance.

A requirement for initial and on-going training for all the types of people working with laboaratory animals is proposed, using the FELASA system as a basis. Whilst this would have cost and adimistrative implications, the benefits that come from better training are likely to outweigh the costs.

A confidential EU database of inforation about project authorisations and ethical review that can be used by applicants, reviewers and regulators is

proposed.  The aim is to encourage best practice and exchange ideas.  This sounds like a very good idea to us.

Finally, it is proposed that each year Member States should collect statistical inforation about the numbers, types, species, etc, of animal experiments and communicate this to the European Comission, who would publish annual EU statistics.  This would include information on the severity levels of procedures.  Whilst this would involve extra work and adimistrative burden for the majority of Member States, publishing reliable statistical data is important for transparency and highly-valued by European politicians and regulators.