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Evaluating opportunities to enhance the implementation of selected welfare and 3Rs provisions of Directive 2010/63

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1. Context and objectives

Adopted in 2010, the Directive 2010/63/EU on the protection of animals used in research has three ambitious goals:

- To ensure harmonization of the legislation on the care and use of animals for scientific purposes to ensure a "level playing field".
- To ensure appropriate standards of welfare through effective application of the 3Rs in the use, care and breeding of animals
- To improve transparency to the general public.

The Directive provides an appropriate framework, which should allow it to achieve its three goals. There is already evidence of positive impact: 3Rs awareness, promotion of culture of care and increasing transparency. There is however potential for further improvement. Full implementation is essential to maximise the benefits intended from it and this is a journey, which requires collaboration between all stakeholders and disciplines.

To further enhance implementation, EFPIA facilitates exchange of good practice between life science community stakeholders through workshops for those directly involved in planning, reviewing and executing research.

This discussion paper summarises recommendations from the second workshop of this kind, which took place on 12 February 2016 in Brussels. This good practice-sharing workshop gathered 45 representatives from public and private research and funding organisations, bio-banks, and breeding establishments to discuss selected provisions that have the potential to promote the 3Rs:

- Choice of methods (Article13)
- Re-use of animals (Article 16)
- Sharing of organs and tissues (Article 18)
- Animal Welfare Bodies (Article 26 and 27)
- Project evaluation (Article 38)
- Retrospective Assessment (Article 39)
- Rehoming (Article 19)

The objective of this document is first and foremost to highlight areas of good practice, which the scientific community can implement to enhance both welfare and quality of science. Some of the recommendations are based on existing good practice in some countries and establishments, and a significant number are addressed to scientific community itself, whether in public or commercial sectors.

However, the implementation of some of the proposed recommendations does require support from third parties, e.g. competent authorities, national animal welfare committees, animal welfare organisations, 3Rs centres, etc. This discussion paper therefore aims at engaging dialogue with these organisations on how to work together to achieve the ambitious goals of the Directive.

2. Abbreviations - Glossary of terms

ARRIVE guidelines	NC3Rs ARRIVE (Animal Research: Reporting of *In Vivo* Experiments) guidelines are intended to improve the reporting of research using animals – maximising information published and minimising unnecessary studies.
AWBs	Animal Welfare Bodies are required in each establishment/organisation to provide internal oversight and guidance on the day-to-day application of the Three Rs, monitor the work in progress and review the outcomes of the work, and may have input into project proposals.
Biobanks	Storage place for biological samples (such as tissue, blood, or DNA) that may be used especially for future medical research
CITES	Convention on International Trade in Endangered Species of Wild Fauna and Flora is an international agreement between governments. Its aim is to ensure that international trade in specimens of wild animals and plants does not threaten their survival.
EDA	Experimental Design Assistant: NC3Rs online tool to guide researchers through the design of their experiments, helping to ensure that they use the minimum number of animals consistent with their scientific objectives, methods to reduce subjective bias, and appropriate statistical analysis.
ESFRI	European Strategy Forum on Research Infrastructures: strategic instrument to foster scientific integration of Europe and to strengthen its international outreach
ETPLAS	European Training Platform for Laboratory Animal Science

	The Platform provides a forum for exchanging information on laboratory animal science education and training therefore helping to establish mutually recognised training courses.
EURL/ECVAM	The European Union Reference Laboratory for Alternatives to Animal Testing , in Directorate-General JRC (see below), promotes the scientific and regulatory acceptance of non-animal tests which are of importance to biomedical sciences and co-ordinates at the European level the independent evaluation of the relevance and reliability of tests for specific purposes. The regulatory acceptance is in the EU is coordinated by the relevant policy Directorate-Generals of the Commission such as DG GROW, ENV and SANTE.
FELASA	Federation of Laboratory Animal Science Associations Represents common interests in the furtherance of all aspects of laboratory animal science (LAS) in Europe and beyond.
FRAME	Fund for the Replacement of Animals in Medical Experiments Its mission is to support the timely development and implementation of scientifically valid methods which will provide reliable data and replace the need for animal experiments
JRC	The Joint Research Centre (JRC) is the European Commission's science and knowledge service which employs scientists to carry out research in order to provide independent scientific advice and support to EU policy.
NC3Rs	UK National Centre for the Replacement, Refinement, Reduction of animals in research
NHPs	Non-human primates: generic term to name various species that are commonly used in biomedical and other research (e.g. Cynomolgus and rhesus macaques)
RSCPA	Royal Society for the Prevention of Cruelty to Animals
SOPs	Standard Operating Procedures
3Rs	1. **Replacement**: methods which avoid or replace the use of animals in research 2. **Reduction**: use of methods that enable researchers to obtain comparable levels of information from fewer animals, or to obtain more information from the same number of animals. 3. **Refinement**: use of methods that alleviate or minimise potential pain, suffering or distress, and enhance animal welfare for the animals used

3. Recommendations to enhance implementation of Directive 2010/63/EU 3Rs provisions

General considerations

In some Member States the implementation of Directive 2010/63/EU has been delayed and in these cases there will be only limited experience with the Directive. Moreover, the implementation of one of the key provisions of the Directive, actual severity assessment and reporting of individual animals was only first carried out in 2015 and binding housing and care standards will only become compulsory in 2017. That means that for many of the provisions it is too early to measure impact. There are however clear indicators of progress in particular where the required practice did not previously exist at national level.

One point raised consistently across all themes is access to information and guidance. There are good guidance documents issued by the European Commission that aren't considered sufficiently accessible, may not have been circulated widely through the individual competent authorities and therefore haven't reached a wide range of users.

There are two recurring recommendations

- For competent authorities to play a more active role in **dissemination (push)** of the EU Commission Guidance documents to all establishments in their Member State.
- There are other useful documents issued from individual competent authorities that might benefit from wider sharing. It was felt a '**one stop' shop** was needed to centralise all information and resources relevant to implementation of the Directive. The European Commission (DG Environment or DG JRC) could provide such one stop shop platform.

Article 13 - Choice of methods (and species)

Access to information and optimisation of internal process were two major themes discussed where choice of methods is concerned.

Area for improvement	**Recommendations**	**Addressee**
Application of local expertise to project evaluation	Voluntary review of licence applications prior to submission to Competent Authority to ensure local expertise and good practice is incorporated. Develop a set of questions to help AWBs critically assess an application. EFPIA could co-ordinate a cross industry/life sciences sector work stream for this.	Establishments EFPIA
Access to expertise in experimental design	Raise awareness of existing resources such as NC3Rs resource EDA through proactive push or one-stop-shop	EU Commission one stop shop Competent authorities, Animal Welfare Bodies
Consistency in species selection	Needs to differ depending on the research area. Overarching principles should be agreed (e.g. through a European Commission expert working group).	European Commission
Lack of evidence base for welfare (refinement) practices	Consider a research funding priority for collaborative projects at EU or national levels	European Commission, Research Funding Organisations
Implementation of publication guidelines e.g. ARRIVE	Education/dissemination to scientists, more consistent application of requirements, publication of negative results to be enhanced	Establishments, Research Funding Organisations, Publishers
Centralised source of 3Rs	EU 3Rs literature resource (i.e. the searching	Awaiting JRC

publications and dissemination	and sifting of publications managed centrally) and dissemination through electronic newsletters. An expert resource to set up 3Rs searches as a new type of service to researchers could be established	conclusions from 3Rs resource survey JRC/ECVAM?

Article 16 - Reuse

There is a continued confusion over definitions of use, reuse and continued use. The Consensus document issued by the Commission is not easy to find, sufficiently disseminated or understood, and additional guidance and examples would be valuable. There are differences in opinion on the benefits of reuse from a welfare perspective.

Areas for improvement	**Recommendation**	**Addressee**
Little awareness of EU commission consensus documents	Competent Authorities to disseminate consensus document to and within all research Establishments. European Commission to make this easier to find as is not located with 'guidance' (One stop shop).	Establishments Competent authorities, European Commission, LAS organisations
Disagreement on value of reuse from welfare perspective	Develop points to consider guidance on the pros and cons of reuse	Scientific Community

Article 18 - Sharing organs and tissues

Lack of awareness about current biobanks was evident in the discussion. The main value for these biobanks is for specific biological materials (rare tissues, such as disease models, or NHPs). For standard material, breeders, or sharing via local networks in house or between establishments is usually sufficient but could be improved. Representatives from bio-banks also confirmed that CITES and animal by-products market legislation is making use of such biobanks difficult, as well as the need to secure appropriate quality of tissues (including impact of naïve vs. non-naïve tissues). From a users perspective concerns arise around lack of standardized processes to ensure appropriate storage and quality of tissue.

Area for Improvement	**Recommendation**	**Addressees**
Local sharing in big establishments	A good practice would be for the establishment licence holder (person responsible for compliance in the establishment) to have accountability for ensuring there are processes for sharing cells and tissues within the Establishment.	Establishments
Little knowledge about existing bio-banks at a national or international level.	Use 'one stop' shop on the Directive (e.g. DG Environment website or ECVAM) to provide a central repository of links to existing Biobanks. Commercial organisations to share good	European Commission, ESFRIs Establishments

	practice on use of surplus animals	
Quality standards	Explore how learning from establishing SOPs and standards for human tissue biobanks could be applied to animal tissue biobanks	ESFRIs, Establishments

Article 26 and 27 - Animal Welfare Body

Workshop participants have unanimously found that these provisions have started to have a positive impact. An observation in many Member States is that welfare is now put even more at the centre of critical considerations about the science and everyday operations. Examples also show impact on scientific considerations where advice of AWBs has led to change of a study protocol or way of working. In some Member States similar structures existed before the new Directive and in these countries the bodies were already conducting many of the tasks of the new AWBs. However, even where similar structures existed under previous legislation the Directive has in some cases provided a catalyst to refresh AWBs and their ways of operating.

Area for Improvement	**Recommendation**	**Addressees**
AWB expertise	Institutions should critically consider AWB membership and structure and whether it is appropriate for the level of complexity of their research activities. They should aim to ensure the breadth of the scientific community is represented as well as mandatory roles, as there is evidence that a breadth of experience and perspectives, from scientists to animal technicians, is useful in driving positive change. Training in experimental design should be recommended – such as that organized by FRAME, NC3Rs, etc. Use of the NC3Rs Experimental Design Assistant should be further promoted. One way of addressing shortage of expertise locally could be for the Competent Authority to facilitate specific thematic workshops at a national level to promote sharing across establishments.	Establishments Competent authorities, national animal welfare committees
Adequate resources and demonstrating value within an institution above and beyond the legal requirement for an AWB	AWB should have clearly established purpose, goals and resources to deliver the objectives approved by the organization. AWBs could collect examples to demonstrate positive and direct impact on ethics-economics-science and culture of care Training of new AWB members: start with implementation of the mandatory module from education and training guidelines (L and E1)	Establishments
AWB support and	National legislation and guidance should be	National welfare

sharing of good practice	scrutinized to ensure that it does not undermine the role and tasks of AWB. National Committee and the Competent Authority Committee could facilitate/sponsor/promote networking between AWBs at regional and national levels to share good practice more broadly. This is has been initiated in some Member States (e.g. UK)	committees, Competent authorities
Dissemination from AWB within an Establishment	Open communication, hosting events e.g. 3Rs poster sessions, awards to recognise and share activities, web pages, targeted communications such as newsletters, e-mail lists	Establishments
Little awareness of EU commission guidance	Competent Authorities to disseminate available guidance to all research Establishments.	Competent authorities

Article 38 - Project evaluation

Project evaluation can be carried out locally and/or centrally by the Competent Authority. It is a complex area and there appears to be limited awareness of existing EU and other National Guidance. There were some comments that well structured templates for licence applications could enhance and assist Project Evaluation by ensuring that the benefits of the research and the harms to the animals can be assessed in a more consistent way.

Area for improvement	**Recommendations**	**Addressees**
Limited awareness of EU Commission and other guidance available on Project Evaluation and aspects such as Harm Benefit Analysis	Competent Authorities to disseminate available guidance to and within all research Establishments. Use 'one stop shop' to provide a central link to UK Home Office/RSPCA/FELASA and other guidance	Competent authorities, Establishments European Commission
Ensuring good practice and knowledge is applied	Voluntary pre-review of license applications by Animal Welfare Bodies prior to submission to Competent Authority to ensure local expertise and good practice is incorporated	Establishments
Accessing relevant literature base	An expert training resource on effective literature searching for 3Rs would be useful as well as potentially a literature searching service that would deliver high quality information and reduce duplication (see also the relevant recommendation under Article 13 section)	ECVAM, ETPLAS 3Rs Centres

Article 39 - Retrospective Assessment

There is not yet enough experience of formal retrospective assessment, but respondents note lack of clear processes nationally and lack of training/guidance. In general a positive impact is anticipated

from the learning generated from these retrospective assessments.

In this section actual severity assessment of individual animals has been included as it is recorded retrospectively although it is not connected to Retrospective Assessment as described in Article 39. The impact of actual individual severity assessment is broader and is an element that can be used to continuously apply the 3Rs.

Areas for improvement	**Recommendations**	**Addressees**
Little awareness of EU commission guidance in this area	Competent Authorities to disseminate available guidance to and within all research Establishments.	Competent authorities, Establishments
Severity assessment of individual animals	Good practice sessions (such as those run at FELASA 2016 annual meeting) for assessing individual severity. Funding for provision of e-learning resources (e.g. developed by FELASA)	EU or national research funding organisations
Lack of resource at end of a project to carry/participate in evaluations	This could be managed via AWB setting milestones for ongoing review for those projects requiring a formal assessment.	Establishments

Article 19 – Rehoming

Some National Authorities and/or Institutions question the value of rehoming.

Areas for improvement	**Recommendations**	**Addressees**
Rehoming processes	Contrast and compare existing policies and processes and provide good practice guidance and define standard processes	Animal Welfare Organisations, Establishments, Veterinarians

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Appendix 1: Relevant extracts from Directive 2010/63

Article 13 (Choice of Methods)

1. Without prejudice to national legislation prohibiting certain types of methods, 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, is recognised under the legislation of the Union.
2. In choosing between procedures, those which to the greatest extent meet the following requirements, shall be selected:
(a) use the minimum number of animals;
(b) involve animals with the lowest capacity to experience pain, suffering, distress or lasting harm;
(c) cause the least pain, suffering, distress or lasting harm; and are most likely to provide satisfactory results.
3. Death as the end-point of a procedure shall be avoided as far as possible and replaced by early and humane end-points. Where death as the end-point is unavoidable, the procedure shall be designed so as to:
(a) result in the deaths of as few animals as possible; and
(b) reduce the duration and intensity of suffering to the animal to the minimum possible and, as far as possible, ensure a painless death.

Article 16 (Reuse)

1. Member States shall ensure that an animal already used in one or more procedures, when a different animal on which no procedure has previously been carried out could also be used, may only be reused in a new procedure provided that the following conditions are met:
(a) the actual severity of the previous procedures was 'mild' or 'moderate';
(b) it is demonstrated that the animal's general state of health and well-being has been fully restored;
(c)the further procedure is classified as 'mild', 'moderate' or 'non-recovery'; and
(d)it is in accordance with veterinary advice, taking into account the lifetime experience of the animal.
2. In exceptional circumstances, by way of derogation from point (a) of paragraph 1 and after a veterinary examination of the animal, the competent authority may allow reuse of an animal, provided the animal has not been used more than once in a procedure entailing severe pain, distress or equivalent suffering.

Article 18 (Sharing of organs and tissues)

Member States shall facilitate, where appropriate, the establishment of programmes for the sharing of organs and tissues of animals killed.

Article 26 (Animal Welfare Bodies)

1. Member States shall ensure that each breeder, supplier and user sets up an animal-welfare body.

2. The animal-welfare body shall include at least the person or persons responsible for the welfare and care of the animals and, in the case of a user, a scientific member. The animal-welfare body shall also receive input from the designated veterinarian or the expert referred to in Article 25.
3. Member States may allow small breeders, suppliers and users to fulfil the tasks laid down in Article 27(1) by other means.

Article 27 (tasks of AWBs)

1. The animal-welfare body shall, as a minimum, carry out the following tasks:
(a) advise the staff dealing with animals on matters related to the welfare of animals, in relation to their acquisition, accommodation, care and use;
(b) advise the staff on the application of the requirement of replacement, reduction and refinement, and keep it informed of technical and scientific developments concerning the application of that requirement;
(c) establish and review internal operational processes as regards monitoring, reporting and follow-up in relation to the welfare of animals housed or used in the establishment;
(d) follow the development and outcome of projects, taking into account the effect on the animals used, and identify and advise as regards elements that further contribute to replacement, reduction and refinement; and
(e)advise on rehoming schemes, including the appropriate socialisation of the animals to be rehomed.
2. Member States shall ensure that the records of any advice given by the animal-welfare body and decisions taken regarding that advice are kept for at least 3 years.
The records shall be made available to the competent authority upon request.

Article 38 (Project Evaluation)

1. The project evaluation shall be performed with a degree of detail appropriate for the type of project and shall verify that the project meets the following criteria:
(a)the project is justified from a scientific or educational point of view or required by law;
(b)the purposes of the project justify the use of animals; and
(c) the project is designed so as to enable procedures to be carried out in the most humane and environmentally sensitive manner possible.
2. The project evaluation shall consist in particular of the following:
(a)an evaluation of the objectives of the project, the predicted scientific benefits or educational value;
(b)an assessment of the compliance of the project with the requirement of replacement, reduction and refinement;
(c)an assessment and assignment of the classification of the severity of procedures;
(d)a harm-benefit analysis of the project, to assess whether the harm to the animals in terms of suffering, pain and distress is justified by the expected outcome taking into account ethical considerations, and may ultimately benefit human beings, animals or the environment;
(e)an assessment of any justification referred to in Articles 6 to 12, 14, 16 and 33; and
(f)a determination as to whether and when the project should be assessed retrospectively.
3. The competent authority carrying out the project evaluation shall consider expertise in particular in the following areas:
(a)the areas of scientific use for which animals will be used including replacement, reduction and

refinement in the respective areas;
(b)experimental design, including statistics where appropriate;
(c)veterinary practice in laboratory animal science or wildlife veterinary practice where appropriate;
(d)animal husbandry and care, in relation to the species that are intended to be used.
4. The project evaluation process shall be transparent.
Subject to safeguarding intellectual property and confidential information, the project evaluation shall be performed in an impartial manner and may integrate the opinion of independent parties.

Article 39 (Retrospective Assessment)

1. Member States shall ensure that when determined in accordance with Article 38(2)(f), the retrospective assessment shall be carried out by the competent authority which shall, on the basis of the necessary documentation submitted by the user, evaluate the following:
(a)whether the objectives of the project were achieved;
(b)the harm inflicted on animals, including the numbers and species of animals used, and the severity of the procedures; and
(c)any elements that may contribute to the further implementation of the requirement of replacement, reduction and refinement.
2. All projects using non-human primates and projects involving procedures classified as 'severe', including those referred to in Article 15(2), shall undergo a retrospective assessment.
3. Without prejudice to paragraph 2 and by way of derogation from Article 38(2)(f), Member States may exempt projects involving only procedures classified as 'mild' or 'non-recovery' from the requirement for a retrospective assessment.

Article 19 (Rehoming)

Member States may allow animals used or intended to be used in procedures to be rehomed, or returned to a suitable habitat or husbandry system appropriate to the species, provided that the following conditions are met:
(a) the state of health of the animal allows it;
(b) there is no danger to public health, animal health or the environment; and
(c) appropriate measures have been taken to safeguard the well-being of the animal



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