Understanding ANIMAL RESEARCH

November 2010

The revised European Directive 2010/63/EU: a guide for UK institutions

Process of revision

The new European Directive 2010/63/EU (to replace EU 86/609) was finalised and came into force across the EU in November 2010. Member States have two years to transpose it into their national systems of legislation. Full implementation of the Directive then starts in January 2013.

The main legally-binding parts of the text are the 'articles' and 'annexes'. The introductory 'recitals' are intended to explain and justify the rest of the Directive, but little weight should be given to the recitals for interpreting the Directive.

Next steps

'Transposition' is the process by which the Directive is converted into new national legislation. In the UK this process can be done through either regulations (simpler and more likely) or through primary legislation (which requires more time in the Houses of Parliament and so introduces more uncertainties). Two years from the date of adoption are allowed for transposition, which the Home Office plans to be completed by summer 2012.

Finally, all other necessary measures must be taken to bring the new legislation into force, such as guidance and administrative measures. It is likely to replace ASPA in January 2013, at which time ASPA is repealed.

Technically, member states should 'align' their legislation with the Directive; this allows only limited variation from the Directive, although countries are encouraged to use their own wording. Therefore the new law could be a consolidated text which is an amalgam of elements of our own 1986 Act, plus some bits of text taken directly from the Directive (eg where the exact wording is important), plus any new text that is required.

Background

EU 86 was revised with the following stated aims:

↘ To 'harmonise' animal research legislation across EU countries, ie to ensure *"a level playing field throughout the EU for industry and the research community"*.

↘ To strengthen the protection of animals used in scientific procedures in line with the EC Treaty of Rome protocol on animal welfare.

↘ To implement fully the principles of the 3Rs (reduction, refinement and replacement of the use of animals used for research).

The principle of harmonising measures to improve animal welfare and the 3Rs was welcome, and there may also be benefits to science from harmonisation. It was probably lobbying from antivivisection organisations which explains why the original Commission proposal included a number of restrictions on research which went beyond improvements in welfare. Most of those proposed restrictions were subsequently amended so that they should not now undermine the EU's ability to undertake research.

For the majority of researchers there should be little change in the ability to carry out animal research in the UK. Indeed, there may be an opportunity to streamline the regulatory system to minimise unnecessary administrative burdens which do not contribute to animal welfare or the 3Rs.

Animal welfare groups agree that across much of Europe the revised Directive is a significant improvement. However they have voiced concerns that the revised Directive could undermine some aspects of the UK regulatory system - and these issues will need to be addressed.

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There has been much pressure from animal protection organisations to enshrine the words *"sentient beings"* across a range of EU legislation. This actual wording does not appear in the legally binding articles, although animals are recognised as having *"capacity to experience pain, suffering, distress or lasting harm"*.

Key elements

The new Directive, now called 2010/63/EU, is considerably longer and more prescriptive than the 1986 Directive. It specifies much more explicitly what is allowed and what is not.

The approach of restricting many activities, such as the use of animals from the wild, consequently requires exemptions. Our hope is that the application of such exemptions will not prove overly bureaucratic, especially where the need for exemption is self-evident (as in the study of wild animals).

The revised Directive contains provisions on the following key areas (amongst many):

Scope: Clearly defined animals and stages covered, with special provisions in certain instances, such as non-human primates (NHPs), dogs and cats, stray and feral, or wild-caught animals.

Purposes and procedures: Clearly defined permissible purposes, with requirements over procedures, such as the application of 3Rs, selection of methods, stipulation of severity, methods of killing, limits to re-use etc.

Establishments: Definitions of breeder, supplier and user, together with general requirements for authorisation, equipment, staffing, record-keeping, care and accommodation, authorised personnel and 'animal welfare bodies'.

Personnel: training, education, supervision and competence with a system of authorisation.

Projects: Require a licence. The application process includes definition and requirements for project evaluation (equivalent to the UK's current 'cost-benefit assessment '), as well as the authorisation process and a requirement for non-technical summaries and (for some projects) retrospective assessment.

Miscellaneous: Includes inspections, reporting, penalties, fees, and confidentiality.

Detailed provisions

Competent authorities

Each Member State must designate one or more 'competent authorities' responsible for the implementation of this Directive.

We expect in the UK that the Home Office will be the competent authority for project evaluation and authorisation, and will delegate these tasks respectively to the Animals (Scientific Procedures) Inspectorate (ASPI), and the Animals (Scientific Procedures) Division (ASPD) licensing division.

There is still debate to be had about whether institutions may be appointed as the competent authority or be delegated for some roles, for example for the carrying out of retrospective reviews.

Stricter national measures

The Directive allows member states to maintain provisions already in force aimed at *"ensuring more extensive protection of animals ... than those contained in this Directive"*.

The intention of this is to avoid countries being forced to 'water down' their existing regulations.

We would expect the Home Office to identify any such provisions in force in the UK, and discuss their continuation (or not) with stakeholders. There are few such measures but some may be significant (eg some aspects of animal caging; use of developmental stages).

Scope

Lower threshold: The Directive has attempted to define lower thresholds of harms to animals. Therefore, the Directive does not apply to *"practices not likely to cause pain, suffering, distress or lasting harm equivalent to, or higher than, that caused by the introduction of a needle in accordance with good veterinary practice."* However this does not constitute satisfactory guidance on non-invasive procedures (in our view), and greater elaboration will be necessary.

The Directive does not apply to a number of situations, including recognised animal husbandry and practices undertaken for the primary purpose of identification of an animal.

Genetic identification: In the light of these lower threshold and husbandry conditions, there is uncertainty where genetic identification sits, and this will need to be more explicit in national legislation.

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Developing forms: Mammalian fetuses are covered *"as from the last third of their normal development"* but eggs are not covered.

Cephalopods: All live cephalopods are now included, and this raises the question of how to avoid infringement through inadvertent harms to minute cephalopods, for example in seawater samples.

Use of animals

There are a number of provisions to define how and what animals are used.

Humane killing: is covered by the Directive (requiring the use of approved techniques and a minimum of pain, suffering and distress), but does not require authorisation as a procedure. The end result could be similar to the existing Schedule 1 of ASPA.

Endangered species: their use is considerably restricted.

Non-human primates: their use in translational or applied research or toxicity testing is restricted to procedures which are *"undertaken with a view to the avoidance, prevention, diagnosis or treatment of debilitating or potentially life-threatening clinical conditions in human beings"*. It is not yet clear how this will work in practice, and there is likely to be considerable discussion and debate, including a Europe-wide working party set up by the Commission. A debilitating clinical condition means *"a reduction of a person's normal physical or psychological ability to function"*.

Basic research, or research aimed at the preservation of the species, is not covered by this restriction.

F2 requirement: whilst there is a timetable to move to the use of only 'F2 NHPs' (those bred from animals themselves bred in captivity), this is dependent on the results of a feasibility study to be conducted by the Commission, *"in consultation with member states and stakeholders"*. The timetable is therefore not set in stone. The pharmaceutical industry sector across Europe is collaborating on determining criteria for this feasibility study.

Procedures

Humane killing: the methods are set out in Annex IV, with the possibility of exemptions for methods where *"on the basis of scientific evidence the method is considered to be at least as humane"*. We will have to negotiate with the Home Office on how these other methods are determined and how the exemptions are applied.

Alternatives: Member States must ensure that, *"wherever possible, a scientifically satisfactory method or testing strategy, not entailing the use of live animals, shall be used instead of a procedure"*. The exact meaning of *"a scientifically satisfactory method or testing strategy"* needs to be properly determined, including practical limitations.

3Rs: as expected, a number of provisions in the Directive require that the 3Rs are fully applied. Examples include the appropriate design of experiments, choice of humane endpoints, and refinement of breeding, accommodation and care, and methods used in procedures.

Anaesthesia: unless it is inappropriate, procedures must be carried out under general or with local anaesthesia or using analgesics or other appropriate methods. The requirement to treat post-anaesthetic pain could cause a significant increase in the use of analgesics for rodents (we would welcome feedback from practitioners on this point).

Severity classification: this is set out in Annex VIII and is analogous to the system used in the UK (with the word *"severe"* used instead of *"substantial"*). How the Home Office intends to transpose this annex is not yet known. We hope more examples will be included, especially at the upper threshold (see below) and shall argue that the application of a severity classification is a matter of professional and scientific judgement.

Upper threshold restriction: a procedure may not be performed if it involves *"severe pain, suffering or distress that is likely to be long-lasting and cannot be ameliorated"*. This clause was subject to some debate in Europe, and the current wording could leave uncertainties over some pain models that are currently undertaken routinely. Given assurances from the Home Office, we trust that the interpretation will be equivalent to our existing restriction in the UK on severe pain or distress which cannot be alleviated.

Re-use: this is restricted to moderate procedures following moderate procedures. The ability to re-use is to be *"in accordance with veterinary advice taking into account the lifetime experience of the animal"*. This should have no impact on current UK practice.

End of the procedure: we hope that implementation of the Directive will be an opportunity for the Home Office to conclude and clarify its work on release from regulation of genetically-altered (GA) mouse strains, using sensible criteria. This will require ongoing input from users.

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Setting free and re-homing animals: these provisions are welcome, but we will have to work with the Home Office to avoid the multiple criteria becoming overly bureaucratic.

Work outside establishments: this will require an exemption, eg for veterinary or wildlife research. We shall argue for this to entail minimal bureaucracy.

Breeders, suppliers and users

Authorisation of establishments: all establishments must be *"authorised by and registered with the competent authority"*. We have no reason to believe that this will lead to any major change in the system of certificates.

Just as can happen now, the competent authority may take action or withdraw the authorisation if the establishment no longer meets requirements. We have been reassured by the HO that this should be subject to an appeal mechanism (that is not specified in the Directive but is assumed under other Community legislation). This is important since there is concern that the relevant article appears to link authorisation of an establishment with compliance of every individual within it.

The Home Office has already improved the Certificate of Designation under the better regulation initiative. However, sensible suggestions for further improvements, either in principle or practice, are welcome.

Requirements for installations and equipment: this may be an opportunity to clarify the use/requirement of current equipment for humidity control. Importantly, relative humidity levels are not specified, but instead there is the sensible generic requirement that it be *"adapted to the species and age groups housed"*.

Care and accommodation: the standards previously in ETS 123 have been made mandatory under Annex III, with variable lead-in times on cage sizes etc. We assume that this annex will be translated directly into the new UK legislation, but we are not yet sure. This is likely to have significant impact on the costs of rodent breeding and bird housing. [Council of Europe ETS 123 is a set of guidelines accepted in 2005 by an EU-wide group of experts as appropriate non-compulsory guidance. It covers all areas of animal rearing and handling].

There are exemptions to the requirement to conform to Annex III *"for scientific, animal welfare or animal health reasons"*. It remains to be determined how such exemptions will be determined and applied. However, we have no reason to anticipate anything unduly restrictive.

For example, we would expect that farm animals (for scientific procedures) could be kept in a farm environment or commercial conditions as necessary, in much the same way as happens currently.

Personnel

Sufficient staff: Member States must ensure that each breeder, supplier and user has *"sufficient staff on site"*. The Home Office recognises that this does not mean a requirement for professional staff to be actually on site 24 hours a day.

Authorisation: there is no mandatory authorisation of persons carrying out or supervising procedures (apparently to reduce the administrative burden and cater for different types of operations). Instead, the requirements are for the competence of staff.

However, there is still a requirement for Member States to ensure, *"through authorisation or by other means"*, that these competence requirements are fulfilled. We expect the Home Office as the competent authority to maintain at least a register of competent individuals. This would allow the sanction of removal from the register for a person found to be of inadequate competence (this is the model used by the General Medical Council to allow doctors to practise). The question of whether a formal personal licence needs to be issued, and if so what details it should include, is open for debate.

Responsibilities: the Directive does not introduce the ASPA concept of 'named persons'. Rather, it requires that each establishment *"has one or several persons on site who shall* ... [undertake various responsibilities] ...".

Whilst some of these responsibilities are equivalent to those of the 'named persons' in UK establishments under ASPA, there is scope to introduce greater flexibility in local arrangements.

The requirement for a person to "be responsible for overseeing the welfare and care of the animals in the establishment" is close to creating an equivalent of the UK certificate holder.

Training: training remains essential, and will be more in the hands of establishments. The Directive stipulates that *"staff shall be adequately educated and trained before they perform any of the following functions:*

a. *carrying out procedures on animals;*
b. *the design of procedures and projects;*
c. *taking care of animals;*
d. *killing animals."*

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One of the responsibilities referred to above (under *"Responsibilities"*) is for a person to *"ensure that the staff are adequately educated, competent and continuously trained and that they are supervised until they have demonstrated requisite competence"*.

In effect, institutions may need to have their own mechanisms to monitor training and link this to competence, if they do not already.

The Directive failed to ensure consistency of training across the EU. So unless the Home Office and its equivalents across the EU voluntarily agree common standards, we will not get over the current restrictions on mobility of research personnel between EU countries. We are encouraging the HO to permit greater mobility for staff.

Animal welfare bodies (AWB)

Note that in the context of the Directive this refers to internal bodies within establishments, and not to external animal welfare groups such as the RSPCA. The AWB would in effect replace the current ERP system.

Make-up: The animal welfare body must 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 body shall also receive input from the designated veterinarian..."*.

Tasks: The animal-welfare body must, 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;

e. advise on rehoming schemes, including the appropriate socialisation of the animals to be rehomed.

Perhaps the most obvious difference here is the omission of an equivalent of the existing function 2 of ERPs, namely examining proposed applications for new project licences and amendments to existing licences before submission to the Home Office. Consistent with this, note that the word *"ethics"* does not occur in relation to AWB functions; rather the emphasis is on welfare. [To avoid duplication of the work of the Home Office Inspector, ERPs should already be focusing on a local perspective]. We anticipate there will be nothing to stop institutions applying any good practice they have learnt from their current ethical review process.

National committee

Each Member State must have a National Committee for the protection of animals used for scientific purposes. A number of different organisations could take on parts of this role, including the national Animal Procedures Committee (APC), but it is far from clear.

The National Committee should *"advise the competent authorities and animal welfare bodies in matters dealing with the acquisition, breeding, accommodation, care and use of animals in procedures and ensure sharing of best practices"*. It must also *"exchange information on the operation of animal welfare bodies and project evaluation and share best practices within the Community"*.

Inspections

The member state must carry out *"regular"* inspections of people and establishments. However, there appears to be a conflict between this requirement, and the minimum requirement to carry them out on (only) *"at least one third of users"*.

In any case, the frequency of inspection must be adapted *"on the basis of a risk analysis for each establishment"*. Various factors are specified, including types and numbers of animals, types and numbers of projects, and previous compliance.

The focus of inspections intended in the Directive is compliance. A considerable number of current UK inspections are valued for the advisory role they play. Some aspect of this will need to be maintained.

Projects

The requirement for projects in the revised Directive is reasonably similar to the current UK system. In short, an application is made which then requires the *"competent authority"* (for us the Home Office, but not the

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institution) to carry out a project evaluation (essentially the same thing as *"ethical review"*, incorporating a harm-benefit assessment) prior to authorisation.

Application: this must include at least:
a. project proposal;
b. non-technical project summary;
c. information on various elements set out in Annex VII (which largely relates to the 3Rs).

Project evaluation: this is the equivalent of the formal cost-benefit assessment, and is intended to ensure that the work is justified and that the 3Rs have been fully applied. Project evaluation is meant to be done with the *"degree of detail appropriate for the type of project"*. However, it needs to be determined how this will be incorporated into UK legislation or guidance, and what it will mean in practice. It is possible this could involve a more explicit risk-based assessment for project licences (with less detail for less sentient animals or minimal harms).

It is a requirement that the overall process for project evaluation is transparent in each member state, so the criteria will need to be set out.

In addition, it must be *"performed in an impartial manner"* and it *"may integrate the opinion of independent parties"*. Our understanding is that both of these functions could be performed by the Home Office Inspector. We do not consider that this constitutes a requirement for input from lay persons, nor from animal protection groups but is there no reason for these to be excluded.

One significant difference is that the severity classification for the project goes with the most severe individual procedure, not (as now) with the average severity across all procedures. It remains to be seen how this will be implemented and what implications it will have.

Simplified administrative procedure: Member States may decide to introduce a simplified administrative procedure for projects containing procedures classified as non-recovery, mild or moderate and not using non-human primates, that are *"necessary to satisfy regulatory requirements, or that are using animals for production or diagnostic purposes with established methods"*. A project evaluation and authorisation is still required, and there appears to be minimal benefit to this.

Retrospective assessment: these are mandatory for *"All projects using non-human primates and projects containing procedures classified as severe"*. The Directive stipulates that *"retrospective assessment shall be carried out by the competent authority"*. However, we are proposing to the HO that much of the function could be delegated to the institution's *"animal welfare body"*, which will be in a better position to know the current standing of any research project within an establishment.

Authorisation decisions: the decision regarding authorisation is to be "taken and communicated to the applicant at the latest within 40 working days from the receipt of the complete and correct application. This time period shall include the project evaluation".

We understand this operates on a stop-the-clock basis. The time limit of 40 days is longer than most applications currently spend at the Home Office. However, there would be a benefit for a minority of projects which may have been subject to greater delays in the past (for example controversial applications on NHPs referred to the APC).

Non-technical project summaries: these will now be mandatory for authorised projects and are to be published by the competent authority. There are clear criteria for the content, including *"information on the objectives of the project, including the predicted harm and benefits and the number and types of animals to be used; [and] a demonstration of compliance with the requirement of replacement, reduction and refinement"*.

However, the non-technical project summary will be *"anonymous and shall not contain names and addresses of the user and its personnel"*. The non-technical summary is to be updated with the results from any retrospective review.

Freedom of Information

There are various safeguards throughout the Directive which protect confidentiality and commercially sensitive information in specific places. However, there is no all-embracing *"confidentiality clause"* such as that which we have in the UK ASPA (Section 24). The Directive specifies only that non-technical summaries shall be published, and nothing is said about the rest of the information in project applications.

We will be negotiating with the Home Office to determine what measures might continue to be necessary to protect confidential information.

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Future negotiations

Over recent years the UK bioscience sector has worked on research policy and legislation issues as a coalition of industry, academia, funding agencies, charities and patient groups. That coalition was important in negotiations over the terms of the final Directive, and will continue to negotiate with the Home Office over transposition. Indeed, a series of meetings is in train to exchange views with the Home Office on how best to promote good science and animal welfare while minimising red tape.

At the same time, we will maintain European networks and try to establish what approach other members states are taking to transposition and implementation.

The Home Office has indicated at this stage that it is likely to carry out certainly one and possibly two consultations. The first is expected in early 2011, so there is reasonable time for us to get input from those affected and develop a position.

Should any institution or individual wish to feed in to these discussions, please contact either Understanding Animal Research, or (for industry) the Association of the British Pharmaceutical Industry, or (for any in the bioscience sector) the Society of Biology's Animal Sciences Group.

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http://www.understandinganimalresearch.org.uk/policy_issues/european_regulation/the_new_directive