



Principles and approaches in ethics assessment

The use of animals in research

Rowena Rodrigues

Trilateral Research & Consulting LLP

June 2015

Annex 1.f

Ethical Assessment of Research and Innovation: A Comparative Analysis of Practices and Institutions in the EU and selected other countries

Deliverable 1.1

This deliverable and the work described in it is part of the project *Stakeholders Acting Together on the Ethical Impact Assessment of Research and Innovation - SATORI* - which received funding from the European Commission's Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 612231



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1 Introduction

This report discusses the use of animals in research. It provides a basic description on the use of animals in research, examines EU legislation for the protection of animals used for scientific purposes, the values and principles prevalent in the area, and key ethical issues. It also looks at the key organisations, institutionalisation, international frameworks and protocols and other relevant issues.

2 Basic description of the field or discipline, incl. disciplines and/or sub-disciplines

This section highlights the nature of the use of animals for research, along with some statistics.

A variety of animal species are used for animal experiments around the world including rats, mice, rabbits, guinea pigs, hamsters, cats, dogs, (mini-pigs), primates, goats, sheep, birds, fish etc.¹ The use of animals in research is particularly considered vital in biomedical research and testing. The UK based website of *Understanding Animals Research* (an animal experimentation community lobbying group) suggests that animals are used in five main areas of biomedical research and product testing:²

- Developing new treatments for diseases or ways of preventing disease
- Basic biological and medical research
- Breeding of laboratory animals (mostly for research and developing new treatments)
- Developing new methods of diagnosis
- Safety testing of non-medical products used in the home, agriculture and industry (no cosmetic or toiletries after 1998).

The *Seventh Report from the European Commission to the Council and the European Parliament on the Statistics on the number of animals used for experimental and other scientific purposes in the Member States of the European Union*³ states:

In the EU, the total number of animals used for experimental and other scientific purposes from the data collected in 2011 in accordance with the provision of the Directive for this report is just under 11,5 million (with data from France from 2010). This is a reduction of over half a million animals used in the EU from the number reported in 2008. As found in previous reports, rodents and rabbits account for 80% of the total number of animals used in the EU. Mice are the most commonly used species with 61% of the total use, followed by rats with 14%. The second most used group of animals was, as in previous years, the cold-blooded animals⁴ which represents almost 12,5%. The third largest group of animals used was birds

¹ Dr Hadwen Trust, "Frequently Asked Questions about the DHT and Alternatives to animal experimentation", <http://www.drhadwentrust.org/about-us/faqs>

² Understanding Animal Research, "Areas of research". <http://www.understandinganimalresearch.org.uk/how/areas-of-research/>

³ European Commission, *Report from the Commission to the Council and the European Parliament, Seventh Report on the Statistics on the Number of Animals used for Experimental and other Scientific Purposes in the Member States of the European Union*, 5 December 2013. COM/2013/0859 final.

⁴ Namely reptiles, amphibians and fish.

with 5,9% of the total use. As stated in the previous three statistical reports no 'Great Apes' were used in experiments in the EU in 2011.⁵

Further, the Seventh Report also states that the Artiodactyla and Perissodactyla group including horses, donkeys and cross-bred animals (Perissodactyla), pigs, goats, sheep and cattle (Artiodactyla) represent only 1.2% of the total number of animals used in the Member States.⁶ Carnivores (which include dogs and cats) represent 0.25% of the total number of animals used and non-human primates represent 0.05% of the animals used in 2011. The number of animals used for toxicological and other safety evaluation amounts to 8.75% of the total (which represents a modest decrease since 2008). The number of animals used for production and quality control of devices for medicine, veterinary medicine and dentistry has decreased by approximately 192,000 animals, but the use of rabbits has increased by more than 81,000 animals for production and quality control of products and devices for human medicine and dentistry.

The Seventh Report also suggests:

Further substantial increases since 2008 have been observed for mice (521,000) and fish (324,000) used in larger numbers for fundamental biological studies. There is also an increase in the use of fish (above 83,000) and birds (above 10,000) for 'other experiments'. Regarding the increase of mice for biological studies of a fundamental nature, Member States indicated that it was due to an increase in research using transgenic mice as specific models for e.g. ocular research, bone metabolism and fertility. The type of studies include LD50, ED50, potency testing and immunogenicity testing, studies in the area of neuroscience, of immunology, studies on physiopathological mechanisms of tumours and research to gain experience for the determination of mechanisms of action of diseases for therapeutic purposes. The increased use of fish in the area of fundamental research was attributed to studies on fish production, genetics, bio-molecular studies, cancer research, physiopathology and diagnosis. Fish have also been used for neurology and cardiovascular studies, and due to the bio-energetic properties of their cardiac cells. The increase in fish numbers in the category of 'other experiments' was attributed to single testing of biocides and to telemetric monitoring of some common species in the environment. Fish are also exclusively used under this heading by some Member states for vaccine studies.⁷

As of 7 November 2014, stem cells have been used to repair damage caused to the brain by Parkinson's disease in rats in Sweden⁸, a new form of Alzheimer's drug has managed to sneak through the blood-brain barrier in monkeys and reduce the levels of harmful amyloid beta protein present,⁹ and a tiny surgical device that could be used to treat a heart defect in children has been successfully trialled in pigs.¹⁰

⁵ European Commission, Seventh Report, op. cit., 2013.

⁶ European Commission, Seventh Report, op. cit., 2013.

⁷ European Commission, Seventh Report, op. cit., 2013.

⁸ BBC News, "Parkinson's stem cell 'breakthrough'", *BBC News*, 7 November 2014. <http://www.bbc.com/news/health-29935449>

⁹ Reardon, Sara, "Alzheimer's drug sneaks through blood-brain barrier", *Nature*, 5 November 2014. <http://www.nature.com/news/alzheimer-s-drug-sneaks-through-blood-brain-barrier-1.16291>

¹⁰ Hodson, Hal, "Heart ops shrink thanks to surgeon in your vein", *NewScientist*, 30 October 2014. <http://www.newscientist.com/article/mg22429935.100-heart-ops-shrink-thanks-to-surgeon-in-your-vein.html#.VFdiEfmsVRp>

Basic biological and medical research uses animals to investigate, for instance, how the human body, its tissues and organs function, in addition to causes of disease. New treatments such as the polio and diphtheria vaccines, insulin for diabetes, and kidney transplants are cited as examples of medical advances supported by animal research.¹¹ Animal research is also considered vital in cases of research into diseases such as AIDS and certain cancers and the development of new diagnostic methods (e.g. scanning to check health of unborn babies).¹² *Understanding Animal Research* suggests that “Safety testing makes up a very small proportion of animal research and is done to guard against products which could cause damage like cancer or birth defects” and based on 2010 figures is evident in sectors such as environment, agriculture, industry, household, foods/food additives.¹³

Genetically modified (GM) animals (e.g. mice and rats) are used in genetic studies. Different types of transgenic animals created (such as transgenic *Drosophila*, transgenic frogs, transgenic fish, transgenic mammals including mice, rats and various livestock animals) have been useful in understanding aspects of gene function and development in these species.¹⁴ Strachan and Read also report that “transgenic sheep and other transgenic livestock animals have been produced largely to serve as bioreactors, whole-animal expression cloning systems in which introduced genes are expressed to give large amounts of therapeutic or commercially valuable gene products”, “but it has been transgenic mice that have been the most useful to biomedical research, both in providing animal models of disease and in permitting the most useful analyses of mammalian gene function.”¹⁵

As one scientist notes, “Genetically engineered animals have opened new frontiers in the study of physiology and disease processes. Mutant animals offer more accurate disease models and increased precision for pathogenesis and treatment studies. Their use offers hope for improved therapy to patients with conditions that currently have poor or ineffective treatments.”¹⁶

Another area of relevance is animal cloning which involves the creation of a genetically identical copy of an animal (frogs, sheep, mice and cows have been cloned). According to *Understanding Animal Research*, “GM animals are the main reason the numbers of experiments in the UK have been rising in the last decade. Genetic modification (mostly of mice) now accounts for half of animal procedures every year in the UK. The largest category of use is breeding (to produce GA animals), accounting for 48% of all procedures (over two million) in 2012. Within this category about one sixth of the animals were in fact genetically normal.”¹⁷ Further, *Understanding Animal Research* states “Over half of all experiments in

¹¹ See RDS: Understanding Animal Research in Medicine and Coalition for Medical Progress, Medical advances and animal research The contribution of animal science to the medical revolution: some case histories, 2007. <http://www.understandinganimalresearch.org.uk/files/7214/1041/0599/medical-advances-and.pdf>

¹²Ibid; Understanding Animal Research, “Development of new diagnostic methods”. <http://www.understandinganimalresearch.org.uk/how/areas-research/development-of-new-diagnostic-methods/>

¹³Understanding Animal Research, “Safety testing of non-medical products”. <http://www.understandinganimalresearch.org.uk/how/areas-of-research/safety-testing-of-non-medical-products>

¹⁴ Strachan, Tom, and Andrew P. Read, *Human Molecular Genetics*, 2nd edition, Wiley-Liss, New York, 1999.

¹⁵ Ibid.

¹⁶ Dennis, Melvin B, “Welfare issues of genetically modified animals”, *ILAR Journal*, 43, 2, 2002, pp. 100-109.

¹⁷Understanding Animal Research, “Breeding and GM mice”. <http://www.understandinganimalresearch.org.uk/how/areas-of-research/breeding-and-gm-mice/>

the UK in 2012 were on GA animals, and most of the GM animals were mice (1.78 million) or fish (169,000). There are almost twice as many procedures involving GM mice than normal mice.”¹⁸ Statistics for the UK on animals used for research in 2012 show:¹⁹

- 4,033,310 animals were used in 2011
- Around half of experiments (48%) were breeding procedures to produce a GM or Harmful Mutant (HM) mouse
- Over 97% of animals used were mice, rats, birds and fish;
- Dogs, cats and primates made up 0.14% of animals used in 2012;
- 48% of experiments were conducted by universities and medical schools, 27% was conducted by industry
- No animals are used for cosmetics testing,
- No animals were used to test finished household cleaners in 2011
- It is illegal to use great apes or wild-caught primates
- It is illegal to use an animal if there is an alternative.

Animals have also been taken to space by scientists. A variety of animals such as mice, dogs, fish, frogs, worms, butterflies, birds have been taken to space for study purposes.²⁰ Non-human primates have also been into space.²¹

Living animals are often used in military medical training both in military laboratories and on training bases.²² People for the Ethical Treatment of Animals (PETA) (an animal rights organisation) reports that “Published experiments and internal documents obtained from the armed forces reveal that U.S. military agencies test all manner of weaponry on animals, from bombs to biological, chemical, and nuclear agents”.²³ A survey of (North Atlantic Treaty Organization) NATO countries revealed that 22 NATO countries including Albania, Belgium, Bulgaria, Croatia, Czech Republic, Estonia, France, Germany, Greece, Hungary, Iceland, Italy, Latvia, Lithuania, Luxembourg, the Netherlands, Portugal, Romania, Slovakia, Slovenia, Spain, and Turkey, do not use animals in military medical training exercises, due to legal prohibitions against animal use and availability of simulation technology.²⁴ Six other NATO countries, Canada, Denmark, Norway, Poland, the US, and the UK, use animals in military medical training.

¹⁸ Ibid.

¹⁹ Understanding Animal Research, “Statistics on animals used for research in 2012”, <http://www.understandinganimalresearch.org.uk/media-library/download/document/98/>

²⁰ NASA, Animals in space. http://www.nasa.gov/audience/forstudents/9-12/features/F_Animals_in_Space_9-12.html; Betancourt, Mark, “On the orbiting of species”, *Air & Space Magazine*, October 2011. <http://www.airspacemag.com/space/on-the-orbiting-of-species-111165162/#ixzz3IwcBGs00>

²¹ NASA, “A Brief History of Animals in Space”, 2 August 2004.

²² See Bender, Bryan, “Military to curtail the use of live animals in medical training”, *The Boston Globe*, 12 November 2014. <http://www.bostonglobe.com/news/nation/2014/11/11/pentagon-takes-major-steps-phase-out-use-live-animals-medical-training/2XOfgaevD80qsHs1A1SbNJ/story.html>

²³ PETA, “The Military’s War on Animals”. <http://www.peta.org/issues/animals-used-for-experimentation/animals-used-experimentation-factsheets/military-war-animals/>

²⁴ Gala, Shalin G., Justin R. Goodman, MAJ Michael, P. Murphy, RADM Marion J. Balsam, “Use of Animals by NATO Countries in Military Medical Training Exercises: An International Survey”, *Military Medicine*, 177, 8, pp. 907, 2012, [p. 907].

One article specifically spotlights the use of animals by the military for ‘live tissue trauma training’ (LTTT) (or ‘combat medic training’) in the US.²⁵ LTTT involves the use of animals (mostly goats and pigs) for direct surgical intervention in which physicians and paramedical personnel (military and civilian) obtain surgical skills by treating severe traumatic injuries inflicted upon animals using surgical instruments or ‘projectile’ methods such as gunshot wounds, (bayonet) stab wounds, (napalm) burns, and amputations. After the animals are deeply anaesthetized, combat-type wounds are inflicted upon them and they are then treated to gain ‘trauma care’ experience not likely to be offered in any other form. After the procedures are completed, the animals are “humanely” euthanised without ever regaining consciousness.²⁶

Though animal research has played an invaluable part in many scientific and medical advances and has its advocates, it has been, and is severely criticised by animal rights supporters and anti-vivisectionist groups who believe that the use of animals in research is cruel and unnecessary. Some objections, from PETA, include: that animals experiments are not relevant to human health nor contribute meaningfully to medical advances; that there is always an end need for human testing; distress caused to animals, and variations in physiological reactions to drugs.²⁷

Animal Rescue Media Education’s (ARME)²⁸ Cruelty-Cutter’s (an app to promote cruelty-free shopping) website suggests,

Animal testing is costly and diverts much needed funds that could go to alternative methods. As a research method there are numerous problems with animal experimentation. The volume of animals needed makes animal-based experiments expensive and cumbersome. Getting the same results reproduced in different labs can be a challenge. These tests depend on researcher evaluation which can be very subjective and results from these tests can be skewed by variations which naturally exist between individual animals. This is no minor drawback—the ability to replicate results of a study is a fundamental hallmark of good research.²⁹

3 EU legislation for the protection of animals used for scientific purposes

This section covers EU legislation for the protection of animals used for scientific purposes.

3.1 Horizontal legislation on the protection of animals used for scientific purposes

- Directive 2010/63/EU on the protection of animals used for scientific purposes

²⁵ Martinic, Gary, “Military ‘live tissue trauma training’ using animals in the US – its purpose, importance and commentary on military medical research and the debate on use of animals in military training”, *Commentary, Journal of Military and Veterans’ Health*, Vol. 20, No. 4, November 2012. <http://jmvh.org/article/military-live-tissue-trauma-training-using-animals-in-the-us-its-purpose-importance-and-commentary-on-military-medical-research-and-the-debate-on-use-of-animals-in-military-training/>

²⁶ Ibid.

²⁷ PETA, “Animal Testing Is Bad Science: Point/Counterpoint”, <http://www.peta.org/issues/animals-used-for-experimentation/animal-testing-bad-science/>

²⁸ ARME is a US bases 501 (c) (3) organisation (non-profit) whose mission is to eliminate the suffering of animals. <http://arme.tv/>.

²⁹ Cruelty-cutter.org, “Animal Testing”. http://cruelty-cutter.org/animal_testing

In Europe, Directive 2010/63/EU on the protection of animals used for scientific purposes³⁰ provides for detailed rules to eliminate disparities between laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes. The Directive recognises animal welfare as a value of the Union that is enshrined in Article 13 of the Treaty on the Functioning of the European Union (TFEU). Recital 12 of the Directive highlights:

Animals have an intrinsic value which must be respected. There are also the ethical concerns of the general public as regards the use of animals in procedures. Therefore, animals should always be treated as sentient creatures and their use in procedures should be restricted to areas which may ultimately benefit human or animal health, or the environment. The use of animals for scientific or educational purposes should therefore only be considered where a non-animal alternative is unavailable. Use of animals for scientific procedures in other areas under the competence of the Union should be prohibited.

This Directive (which revised Directive 86/609/EEC on the protection of animals used for scientific purposes) was adopted on 22 September 2010 and is firmly based on the principle of the Three Rs: to replace, reduce and refine the use of animals used for scientific purposes.

Subject matter and scope

This Directive establishes measures for the protection of animals used for scientific or educational purposes. To that end, it lays down rules on the following:

- The replacement and reduction of the use of animals in procedures and the refinement of the breeding, accommodation, care and use of animals in procedures;
- The origin, breeding, marking, care and accommodation and killing of animals;
- The operations of breeders, suppliers and users;
- The evaluation and authorisation of projects involving the use of animals in procedures.

The Directive, which has a wide scope, applies where animals are used or intended to be used in procedures, or bred specifically so that their organs or tissues may be used for scientific purposes and applies until the animals referred to in the first subparagraph have been killed, rehomed or returned to a suitable habitat or husbandry system. Article 2 of Directive 2010/63/EU provides that Member States may, while observing the general rules laid down in the TFEU, maintain provisions in force on 9 November 2010, aimed at ensuring more extensive protection of animals falling within the scope of the Directive than those contained in it. Member States were to notify the Commission about such national provisions before 1 January 2013 and the Commission was to bring them to the attention of other Member States. The Commission provides a listing of Member State authorities for Directive 2010/63/EU.³¹ It lays down minimum standards for housing and care, regulates the use of animals through a systematic project evaluation requiring *inter alia* assessment of pain, suffering distress and lasting harm caused to the animals. It requires regular risk-based inspections and improves

³⁰ European Parliament and of the Council, Directive 2010/63/EU on the protection of animals used for scientific purposes, 22 September 2010. <http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32010L0063>

³¹ European Commission, Animals used for scientific purposes. http://ec.europa.eu/environment/chemicals/lab_animals/ms_en.htm

transparency through measures such as publication of non-technical project summaries and retrospective assessment.

Principle of replacement, reduction and refinement (Article 4)

Article 4 of the Directive states:

- Member States shall 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.
- Member States shall ensure that the number of animals used in projects is reduced to a minimum without compromising the objectives of the project.
- Member States shall ensure refinement of breeding, accommodation and care, and of methods used in procedures, eliminating or reducing to the minimum any possible pain, suffering, distress or lasting harm to the animals.
- This Article shall, in the choice of methods, be implemented in accordance with Article 13.

Purposes of procedures

Procedures may be carried out for the following purposes only: (a) basic research; (b) translational or applied research with any of the following aims: (i) the avoidance, prevention, diagnosis or treatment of disease, ill-health or other abnormality or their effects in human beings, animals or plants; (ii) the assessment, detection, regulation or modification of physiological conditions in human beings, animals or plants; or (iii) the welfare of animals and the improvement of the production conditions for animals reared for agricultural purposes; (c) for any of the aims in point (b) in the development, manufacture or testing of the quality, effectiveness and safety of drugs, foodstuffs and feed-stuffs and other substances or products; (d) protection of the natural environment in the interests of the health or welfare of human beings or animals; (e) research aimed at preservation of the species; (f) higher education, or training for the acquisition, maintenance or improvement of vocational skills; (g) forensic inquiries.

The Directive prescribes the methods of killing, regulates the use of endangered species, non-human primates, animals taken from the wild, animals bred for use in procedures, and stray and feral animals of domestic species. The Directive contains provisions on procedures (Chapter III) including choice of methods, anaesthesia, classification of severity of procedures, reuse, end of the procedure, sharing organs and tissues, and setting free of animals and rehoming.

The Directive also sets authorisation requirements in Chapter IV. Section 1 deals with: requirements for, and authorisation of breeders, suppliers and users, suspension and withdrawal of authorisation, requirements for installations and equipment, competence of personnel, specific requirements for personnel, designated veterinarian, animal-welfare body and its tasks, the breeding strategy for non-human primates, scheme for rehoming or setting free of animals, animal records, information on dogs, cats and non-human primates, marking and identification of dogs, cats and non-human primates and care and accommodation. Section 2 deals with inspections by the Member States and controls of Member State inspections.

Section 3 deals with requirements for projects, project authorisation (which specifies that projects are not to be carried out without prior authorisation from the competent authority. Projects have to be carried out in accordance with the authorisation, or in accordance with the application sent to the competent authority or decision taken by the competent authority). Member States have to ensure that no project is carried out unless it is favourably evaluated. The Directive also contains provisions on application for project authorisation, project evaluation, retrospective assessment, granting of project authorisation, authorisation decisions, simplified administrative procedure³², non-technical project summaries, amendment, renewal and withdrawal of a project authorisation (where change of the project may have a negative impact on animal welfare) and documentation retention requirements.

The Directive calls for a ‘comprehensive project evaluation’ that takes into account ethical considerations in the use of animals, forms the core of project authorisation, and ensures the implementation of principles of replacement, reduction and refinement in projects. The evaluation has to be performed with a degree of detail appropriate for the type of project, and must 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. The project evaluation consists 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. The evaluation process has to be transparent and subject to safeguarding intellectual property and confidential information, it must be performed in an impartial manner and may integrate the opinion of independent parties.

The Directive also recommends avoidance of duplication of procedures across Member States and advocates the use of alternative approaches that do not involve the use of animals, use fewer animals, or which entail less painful procedures. The development, validation and implementation of alternative methods is promoted through a Union Reference Laboratory³³ for the validation of alternative methods supported by laboratories within Member States.

The Directive provides for national committees for the protection of animals used for scientific purposes. These committees advise the competent authorities and animal-welfare bodies on matters dealing with the acquisition, breeding, accommodation, care and use of animals in procedures and ensure sharing of best practice and exchange information on the

³² 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 which use animals for production or diagnostic purposes with established methods.

³³ See EURL-ECVAM in regional organisations table.

operation of animal-welfare bodies and project evaluation, and share best practice within the Union.

Notable is also Annex III of the Directive which sets out the requirements for establishments and for the care and accommodation of animals.

- Consolidated Commission Implementing Decision 2012/707/EU as corrected by Decision 2014/11/EU

This Decision sets out a common format for submitting information on the use of animals for scientific purposes as referred to in paragraphs 1, 2, and 3 of Article 54 of Directive 2010/63/EU. The new system will allow the Commission to assess effectiveness of the implementation of the legislation and help ensure consistency in its application. The first data under the new statistical reporting format was to be collected from 1 January 2014. The Seventh Statistical Report will follow the format of all previous reports.

- Commission Implementing Decision of 14 November 2012 establishing a common format for the submission of the information pursuant to Directive 2010/63/EU of the European Parliament and of the Council on the protection of animals used for scientific purposes (notified under document C(2012) 8064)³⁴
- Commission Implementing Decision of 20 December 2013 correcting Annex II to Implementing Decision 2012/707/EU establishing a common format for the submission of the information pursuant to Directive 2010/63/EU of the European Parliament and of the Council on the protection of animals used for scientific purposes (notified under document C(2013) 9220)³⁵
- Recommendation 2007/526/EC

The Recommendation (adopted on 18 June 2007)³⁶ introduces guidelines for the accommodation and care of animals used for experimental and other scientific purposes. This Recommendation compliments Annex III of Directive 2010/63/EU, and aligns with EC legislation with the revised Council of Europe guidelines (Appendix A of Convention ETS 123), on accommodation and care of laboratory animals.

3.2 Other related legislation

- Council Decision 1999/575/EC³⁷

³⁴European Commission, *OJ L* 320, 17.11.2012, p. 33–50. <http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32012D0707>

³⁵European Commission, *OJ L* 10, 15.1.2014, p. 18–31. <http://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX:32014D0011>

³⁶ European Commission, Commission Recommendation of 18 June 2007 on guidelines for the accommodation and care of animals used for experimental and other scientific purposes (notified under document number C(2007) 2525), *OJ L* 197, 30 July 2007, pp. 1-89.

³⁷ Council of the European Union, Council Decision of 23 March 1998 concerning the conclusion by the Community of the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes, *OJ L* 222, 24 August 1999, pp. 0029 – 0030.

This Decision makes the European Community party to the Council of Europe Convention ETS 123 on the protection of animals used for experimental and other scientific purposes. The contents of the Convention are practically identical to that of Directive 86/609/EEC.

- Council Decision 2003/584/EC³⁸

Linked to the Council Decision 1999/575/EC (above), this Decision 'ratifies', on behalf of the Community, the possibility of updating the appendices of the Council of Europe Convention ETS 123 in a more simplified manner, known as a 'protocol of amendment'. The provisions contained in the Appendices to the Convention are of a technical nature and should reflect the latest scientific and technical developments and results in the research within the fields covered.

4 Values and principles

As shown in the previous section, Directive 2010/63/EC specifies the following criteria as a precondition for a positive evaluation³⁹ of projects: (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. These criteria go beyond the Three Rs. Research sponsors need to justify the use of animals; this is quite important from the ethical point of view. Before the Three Rs can be applied, it must be shown that the research has such a high aim that the use of animals can be justified.

The Three Rs are guiding principles that form the basis of the human use of animals in scientific research (and upon which Directive 2010/63/EU is firmly based). In 1959, Russell and Burch published *The Principles of Humane Experimental Technique* in which they stated that all animal experiments should incorporate, as far as possible **Replacement, Reduction and Refinement** as key strategies of a systematic framework aimed at achieving the goal of humane experimental techniques. Russell and Burch saw replacement as the ultimate goal for laboratory animal based research, education and testing, with reduction and refinement being more readily achievable in the short term.

Replacement refers to methods, strategies or approaches that do not involve the use of live animals. It can be achieved through the use of the following and their combinations:

- *In vitro* systems using tissues, whole cells or parts of cells
- Systems based on biochemical approaches, i.e. using synthetic (macro) molecules as proxies of (reactive) toxicity targets. Such methods are referred to as "*in chimico*"
- Computer-based models and approaches – often termed *in silico*
- Use of 'omics' technologies (e.g. transcriptomics, proteomics and metabonomics)

³⁸ Council of the European Union, Council Decision of 22 July 2003 concerning the conclusion of the Protocol of Amendment to the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes, *OJ L* 198, 6 August 2003, pp. 10–12.

³⁹ Project evaluation is discussed in Section 2 of this report.

- Non-testing approaches such as 'read-across' technique.

Reduction covers any approaches that lead to fewer animals being used to achieve the same objective, including maximising the information obtained per animal, reducing the number of animals used in the original procedure and/or limiting or avoiding the subsequent use of additional animals. **Refinement** signifies the modification of procedures or husbandry and care practices from the time an experimental animal is born till its death so that pain, suffering and distress is minimised and its wellbeing is enhanced.

The Three Rs are present in the EU legislation in spirit, since 1986, when the first EU legislation for the protection of animals used for experimental and other scientific purposes was adopted. The Three Rs are widely accepted by the international scientific community.⁴⁰ Even those opposed to the use of animals in scientific procedures agree with the principle of the Three Rs, though express concerns that they are not always implemented.⁴¹ Other reservations expressed about the three Rs include the concern that “reduction and refinement tacitly acknowledge that animals should continue to be used”;⁴² that “refinement tended to be overlooked and that better use could be made of research into animal cognition”.⁴³ Despite this, the Three Rs seem to have had a strong international influence on the debate on animal experiments.⁴⁴

5 Ethical issues

The Nuffield Council *Report on the Ethics of Research Involving Animals* (2005) discusses and summarises four views on the ethics of animal research:⁴⁵

- **The ‘anything goes’ view** (from this viewpoint, if humans see value in research involving animals, then it requires no further ethical justification)
- **The ‘on balance justification’ view** (which argues that although research involving animals has costs to animals, which must be taken seriously in moral reasoning, the benefits to human beings very often outweigh those costs in moral terms)
- **The ‘moral dilemma’ view** (which argues that most forms of research involving animals pose moral dilemmas: according to the current scientific approach the use of animals is necessary to comply with the moral imperative to cure human disease and to save human lives)
- **The ‘abolitionist’ view** (according to this, humans experiment on animals not because it is right but because they can).

Ormandy and Schuppli discuss and review the factors that previous literature has shown to influence people’s attitudes towards animals, and animal-based research specifically: personal

⁴⁰ UK Select Committee on Animals in Scientific Procedures Report, 2002. <http://www.publications.parliament.uk/pa/ld200102/ldselect/ldanimal/150/15004.htm>

⁴¹ UK Select Committee, op. cit., 2002

⁴² UK Select Committee, op. cit., 2002

⁴³ UK Select Committee, op. cit., 2002

⁴⁴ UK Select Committee, op. cit., 2002

⁴⁵ Nuffield Council on Bioethics, *The ethics of research involving animals*, Nuffield Council on Bioethics, May 2005, p. 244

and cultural characteristics, animal characteristics, and research characteristics.⁴⁶ The personal characteristics that influence people's attitudes towards animals, and animal-based research include: age, sex, rural versus urban background, experience of animals/pet ownership, religion, personality, vegetarianism and animal or environmental advocacy, and belief in animal mind. The animal characteristics that contribute to variation in people's attitudes include species, sentience, neoteny⁴⁷/appeal and genetic modification.⁴⁸ The research characteristics include: the purpose of the research, the level of invasiveness (or harm) that the animal will experience, and availability of non-animal alternatives.⁴⁹ Ormandy and Schuppli also suggest that other variables such as the effect of social media and the living conditions of laboratory animals affect people's attitudes towards animals, or animal research.⁵⁰ Ormandy and Schuppli conclude, that "understanding public attitudes toward the use of animals in research will facilitate the growing trend toward more openness and democratization of scientific research, and ensure that scientific practice (including animal research) remains in step with societal values".⁵¹

We next list and briefly discuss ethical issues most often discussed in the literature on the use of animals in research and animal testing.

5.1 Inability of animals to consent to testing

One of the main ethical issues is the inability of animals to consent to their use in research and testing. While humans have the ability to make informed choices about participation in research and testing, the same is not true for animals. One of the arguments used to justify animal research is that animals are not rational, autonomous beings and that as long as experiments are humane,⁵² there is nothing unethical about using animals in research.⁵³ Sapontzis makes the case that "guardians who understand the animals' interests and are intent on protecting and furthering those interests should be assigned to protect the animals" and that it would be their responsibility to ensure that research "either was innocuous to the animals, was intended to be therapeutic for them, or provided them adequate compensation. Since a primary reason for doing laboratory research on animals is that the research procedure is detrimental to the interests of the research subjects, empowering animal guardians would drastically curtail laboratory animal research".⁵⁴

⁴⁶ Ormandy, Elisabeth H., and Catherine A. Schuppli, "Public Attitudes toward Animal Research: A Review", *Animals*, 4 (3), 2014, pp. 391-408.

⁴⁷ In this context, this refers to the retention of a neonatal appearance.

⁴⁸ Ormandy and Schuppli, op. cit., 2014, p. 397

⁴⁹ Ormandy and Schuppli, op. cit., 2014, p. 398

⁵⁰ Ormandy and Schuppli, op. cit., 2014, p. 399

⁵¹ Ormandy and Schuppli, op. cit., 2014, p. 402

⁵² The Oxford Dictionary defines humane as having or showing compassion or benevolence. It also refers to inflicting the minimum of pain.

⁵³ Sapontzis, S.F., "Animal Experimentation Is Unethical", 2005. http://teacherweb.com/TX/TomballMemorialHighSchool/Campese/Animal_Experimentation_Is_Unethical.pdf

⁵⁴ Ibid.

5.2 Pain, suffering, distress, harm to animals

Regan speaks of the “the pulsing pain of the chimp with electrodes planted deep in her brain”.⁵⁵ Animal experiments are wide-ranging and involve: safety (toxicity) testing, disease/wound infection and healing, application of skin/eye irritants, food/water/sleep deprivation, brain damage, surgical damage, induced organ failure and genetic modification.⁵⁶

While efforts can be made to minimise the pain, suffering and distress caused to animals participating in the research process (e.g. through the use of anaesthesia and other pain alleviation methods), pain is often unavoidable and not completely preventable.

There is also the problem of the “lack of ethical self-examination” which is “common and generally involves the denial or avoidance of animal suffering, resulting in the dehumanization of researchers and the ethical degradation of their research subjects”.⁵⁷ One article by Animal Aid reports that the ‘Cumulative Severity’ report⁵⁸ published in November 2013 “revealed a high level of desensitisation amongst the researchers whose views it sought and who are licensed to inflict substantial suffering on monkeys, often for years on end”.⁵⁹

5.3 Misleading nature and unreliability of animal experiments

Animal Aid - an animal rights group - also highlights that “animal experiments are unreliable and can be dangerously misleading because animals’ bodies are different from ours, and they don’t get the same diseases as we do.”⁶⁰ One of the examples cited in support of this argument is the case of the TGN1412 (‘elephant man’ drug) disaster that left six men with organ failure after tests on monkeys failed to predict these effects.

5.4 Unnecessary use

The unnecessary use of animals is an ethical concern due to its effects upon not only animals but also researchers using animals for experimentation purposes. The frequency and routineness of experimenting on animals often has a desensitising impact upon the researchers involved, may perpetuate the use of animals for experimentation and also somehow lead to a lack of self-examination on the part of the researchers. It is pertinent to note what Regan states:

⁵⁵ Regan, T., “A case for animal rights”, in M.W. Fox & L.D. Mickley (eds.), *Advances in animal welfare science*, The Humane Society of the United States, Washington DC, 1986/87, pp. 179-189.

⁵⁶ Dr Hadwen Trust, “Frequently Asked Questions about the DHT and Alternatives to animal experimentation”, <http://www.drhadwentrust.org/about-us/faqs>

⁵⁷ Gluck, John P., & Steven R. Kubacki, “Animals in Biomedical Research: The Undermining Effect of the Rhetoric of the Besieged”, *Ethics and Behaviour*, Vol. 1, Issue 3, 1991, pp.157-173.

⁵⁸ The Animal Procedures Committee, “Review of the Assessment of Cumulative Severity and Lifetime Experience in Non-human Primates Used in Neuroscience Research”, Report of the Animal Procedures Committee’s Primate Subcommittee Working Group Chaired by Professor John Pickard FMedSci, November 2013.

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/261687/cs_nhp_review_FINAL_2013_corrected.pdf

⁵⁹ Animal Aid, “Insensitivity of Primate Researchers Exposed by Government Committee”, 5 August 2014. http://animalaid.org.uk/h/n/news/news_experiments/all/3132/

⁶⁰ Animal Aid, “Killing Animals and Humans”.

<http://www.animalaid.org.uk/h/n/CAMPAIGNS/experiments/ALL/730/>

Lab animals are not our tasters; we are not their kings. Because these animals are treated routinely, systematically as if their value were reducible to their usefulness to others, they are routinely, systematically treated with a lack of respect, and thus are their rights routinely, systematically violated. This is just as true when they are used in trivial, duplicative, unnecessary or unwise research as it is when they are used in studies that hold out real promise of human benefits.⁶¹

6 Organisations

This section lists the major international, regional and national organisations that are involved in encouraging ethical animal use principles and policies, use and promotion of alternative methods of animal testing, investigation and political lobbying on animal use in research, formulating policy and regulating animal use in research.

Name	Aim, vision, objective	Activities	Web link
International Collaboration on Alternative Test Methods (ICATM)	The framework for ICATM was developed through a collaboration involving ICCVAM, the EURL ECVAM, the Japanese Centre for the Validation of Alternative Methods (JaCVAM), and Health Canada. The purpose of the framework is to promote consistent and enhanced voluntary international cooperation, collaboration, and communication among national validation organisations.	<ul style="list-style-type: none"> Establishing international cooperation validation studies, independent peer review, and development of harmonized recommendations to ensure that alternative methods/strategies are more readily accepted worldwide Establishing international cooperation necessary to ensure that new alternative test methods/strategies adopted for regulatory use provide equivalent or improved protection for people, animals, and the environment, while replacing, reducing, or refining (causing less pain and distress) animal use whenever scientifically feasible. 	http://ntp.niehs.nih.gov/pubhealth/evalatm/iccvam/international-partnerships/index.html
The Interagency Coordinating	To establish, wherever feasible, guidelines, recommendations, and	<ul style="list-style-type: none"> Facilitating interagency and international collaborations 	http://ntp.niehs.nih.gov/pubhealth/evalatm/iccvam/index.html

⁶¹ Regan, T., "A case for animal rights", in M. W. Fox & L.D. Mickley (eds.), *Advances in animal welfare science*, The Humane Society of the United States, Washington DC, 1986/87, pp.179-189, [p. 188].

Name	Aim, vision, objective	Activities	Web link
Committee on the Validation of Alternative Methods (ICCVAM)	regulations that promote the regulatory acceptance of new or revised scientifically valid toxicological tests that protect human and animal health and the environment while reducing, refining, or replacing animal tests and ensuring human safety and product effectiveness.	promoting the development, regulatory acceptance, and use of alternative tests that encourage the reduction, refinement, or replacement of animal test methods <ul style="list-style-type: none"> • Providing guidance to test method developers • Evaluating recommendations from expert peer reviews of alternative toxicological test methods and making recommendations on the use of reviewed test methods to appropriate federal agencies. 	
International Council for Laboratory Animal Science (ICLAS)	Advancing human and animal health by promoting the ethical care and use of laboratory animals in research worldwide.	A world-wide resource for laboratory animal science knowledge; advocate for the advancement of laboratory animal science in developing countries and regions; source of laboratory animal science guidelines and standards, and as general laboratory.	http://iclas.org/

Table 1: Overview of international organisations

The following table presents an overview of regional organisations:

Name	Aim, vision, objective	Activities	Web link
Federation of European Laboratory Animal Science Associations (FELASA)	FELASA represents common interests in the furtherance of all aspects of laboratory animal science (LAS) in Europe and beyond. Advocates responsible scientific conduct with animals in the life sciences with particular emphasis on ensuring animal welfare.	FELASA publishes guidelines, recommendations and policy documents on topics relevant for laboratory animal science. FELASA maintains relations with national, international and governmental bodies concerned with laboratory animal science in Europe, notably the Council of Europe, the European Commission and European Parliament and continuously seeks collaborations with laboratory animal science	http://www.felasa.eu/

Name	Aim, vision, objective	Activities	Web link
		associations outside Europe. FELASA organises triennial international congresses.	
The European Union Reference Laboratory for alternatives to animal testing (EURL-ECVAM)	<ul style="list-style-type: none"> To promote the scientific and regulatory acceptance of non-animal tests which are of importance to biomedical sciences, through research, test development and validation and to establish a specialised database service to co-ordinate at the European level the independent evaluation of the relevance and reliability of tests for specific purposes. 	The validation of methods which reduce, refine or replace the use of animals for safety testing and efficacy/potency testing of chemicals, biologicals and vaccines. Research laboratories are able to submit to EURL ECVAM for scientific validation the alternative methods to animal testing that they have developed. EURL ECVAM also promotes the development and dissemination of alternative methods and approaches, their application in industry and their acceptance by regulators.	https://eurl-ecvam.jrc.ec.europa.eu/
Eurogroup for Animals	Building a Europe that cares for animals	Animal welfare organisation at EU level and represent animal welfare interests on many EU advisory committees and consultation bodies.	http://eurogroupforanimals.org/
European Partnership for Alternative Approaches to Animal Testing (EPAA)	The vision of EPAA is the replacement, reduction and refinement (3Rs) of animal use for meeting regulatory requirements through better and more predictive science.	EPAA is a voluntary collaboration between the European Commission, European trade associations, and companies from seven industry sectors. The partners have committed to pooling knowledge and resources to accelerate the development, validation and acceptance of alternative approaches to further the replacement, reduction and refinement (3Rs) of animal use in regulatory testing.	http://ec.europa.eu/enterprise/epaa/index_en.htm

Table 2: Overview of regional organisations

The following table presents an overview of national level organisations:

Name	Aim, vision, objective	Activities	Web link
National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs)	UK-based scientific organisation dedicated to replacing, refining and reducing the use of animals in research and testing (the 3Rs)	<ul style="list-style-type: none"> • Funding research and early career development. Commercialisation and facilitating technology partnering in the 3Rs through the open innovation programme, CRACK IT. • Provision of evidence base for changes in policy, practice and regulation through data sharing and knowledge exchange, and dissemination. • Provision of 3Rs peer review and advice service to the UK's major funding bodies including the MRC, BBSRC, Wellcome Trust, and AMRC member charities. 	http://www.nc3rs.org.uk/
British Union for the Abolition of Vivisection (BUAV)	Single-issue organisation campaigning to create a world where nobody wants or believes we need to experiment on animals.	Undercover investigations, political lobbying, promotion of cruelty free products, legal and scientific expertise, media activities	http://www.buav.org/
Dr Hadwen Trust for Humane Research	A UK non-animal medical research charity, its aim is to support and promote medical research that has the potential to replace experiments on animals.	The DHT does not fund any work that aims to 'Reduce' or 'Refine' animal use.	http://www.drhadwentrust.org
Institute for Laboratory Animal Research (ILAR), USA	To evaluate and to report on scientific, technological, and ethical use of animals and related biological resources, and of non-animal alternatives in non-food settings, such as research, testing, education, and production of pharmaceuticals.	ILAR evaluates and encourages the use, development, and validation of non-animal alternatives. ILAR provides independent, objective advice to the federal government, to the international biomedical community, and to the public through reports of expert committees, web-based resources, and other means of communication. It is a unit in the Division on Earth and Life Studies of the National Research Council.	http://dels.nas.edu/ilar
Biotechnology	One of 7 Research Councils	Research Funding. The	http://www.bbsrc.ac.u

Name	Aim, vision, objective	Activities	Web link
and Biological Sciences Research Council (BBSRC), UK	that work together as Research Councils UK (RCUK). Its mission: to promote and support, by any means, high-quality basic, strategic and applied research and related postgraduate training relating to the understanding and exploitation of biological systems and to advance knowledge and technology. The BBSRC has a policy on the use of animals in research. ⁶²	BBSRC supports the continued use of animals in scientific research, but only when strict conditions are met. All BBSRC grant awards are made on the absolute condition that no work that is controlled by the Animals (Scientific Procedures) Act 1986 (ASPA, amended in 2012) will begin until the necessary licences required under the Act have been obtained. BBSRC supports researchers in providing excellent care and welfare standards for animals used in research. BBSRC is a signatory, with other funding bodies, to two guidance documents ‘Responsibility in the Use of Animals in Research’ and ‘Sharing and Archiving of Genetically Altered Mice’. BBSRC funds research to replace, refine and reduce (3Rs) the numbers of animals used in research. It is a co-funder of the National Centre for the 3Rs (NC3Rs) which provides a focus for the promotion, development and implementation of the 3Rs in animal research and advises BBSRC on 3Rs issues.	k/home/home.aspx
Hastings Centre (USA)	Independent, nonpartisan, and non-profit bioethics research institute founded in 1969. The Center's mission is to “address fundamental ethical issues in the areas of health, medicine, and the environment as they affect individuals, communities, and societies. One of the selected issues it focuses on	It launched a project on Ethics of Medical Research with Animals: Science, Values, and Alternatives in June 2011. The goal was to bring together people with different points of view and different areas of expertise on animal research ethics and alternative models to share their knowledge, exchange ideas and insights, and produce unbiased	http://www.thehastingscenter.org/

⁶² BBSRC, The use of animals in research – the position of the Biotechnology and Biological Sciences Research Council (BBSRC), January 2013. http://www.bbsrc.ac.uk/web/FILES/Policies/animals_in_research.pdf

Name	Aim, vision, objective	Activities	Web link
	is animal research ethics”.	educational resources. A multidisciplinary workshop, held at Yale University in November 2011, explored ethical and scientific issues in animal research and the use of alternatives. From the workshop, Hastings Center editors produced a set of educational materials for biomedical researchers, scholars, students, commentators in ethics and animal research, Institutional Animal Care and Use Committees, policymakers, and journalists who follow animal research issues. One of these resources is a Hastings Center special report, "Animal Research Ethics: Evolving Views and Practices," written by workshop participants. ⁶³ Another is a website: www.animalresearch.thehastingscenter.org .	
Animal Aid	The UK's largest animal rights group and one of the longest established in the world, having been founded in 1977.	Campaign against all forms of animal abuse and promote a cruelty-free lifestyle. We investigate and expose animal cruelty, and our undercover investigations and other evidence are often used by the media, bringing these issues to public attention.	http://www.animalaid.org.uk
Society of Biology Animal Science Group, UK	Special Interest Group (SIG) of the Society of Biology, representing the broad spectrum of UK bodies actively involved in supporting, formulating policy or directly involved in research involving animals.	Contributes to the UK Bioscience Sector Coalition (UKBSC) on options for implementation of the revised ASPA. Written to the Home Office expressing overarching objectives that animal welfare, the 3Rs, public confidence and high quality biology should be	https://www.societyofbiology.org/policy/asn

⁶³ Gilbert, Susan, Gregory E. Kaebnick and Tomas H. Murray (eds.), *Animals Research Ethics: Evolving Views and Practices*, A Hastings Center Special Report, 2011. http://www.thehastingscenter.org/uploadedFiles/Publications/Special_Reports/AnimalResearchEthics.pdf

Name	Aim, vision, objective	Activities	Web link
		<p>supported by the new legal framework.</p> <p>Submissions on the transposition and implementation of the new Directive 2010/63/EU, as part of the UKBSC and in recent years has been consulted on a wide range of issues including the Home Office IT strategy, the Hampton Review and Defra's proposals for veterinary checks on rabies-susceptible animals at border inspection posts.</p>	
National Anti-Vivisection Society (NAVS), UK	Organisation campaigning against animal experiments	Producing detailed scientific reports highlighting the futility of vivisection; lobbying in Parliament; organising the rallies against vivisection; developing the Lord Dowding Fund and adding two new bodies to the group - the Animal Defenders and Animal+World Show; putting NAVS Field Officers undercover inside the animal laboratories.	http://www.navs.org.uk/
Fund for the Replacement of Animals in Medical Experiments (FRAME), UK	To eliminate the need to use laboratory animals in any kind of medical or scientific procedures, but FRAME accepts that a total end to their use cannot be achieved immediately.	Investigating and developing new methods at the forefront of science. Collaborating with other organisations, industry and laboratories across a wide range of biological and medical fields.	http://www.frame.org.uk/
Understanding Animal Research (<i>formed by merger of the Research Defence Society and the Coalition for Medical Progress</i>)	Advocacy group that aims to achieve broad understanding of the humane use of animals in medical, veterinary, scientific and environmental research in the UK.	Providing information and educational materials based on thorough research and understanding of the facts, historical and scientific.	http://www.understandinganimalresearch.org.uk/
Royal Society for Prevention of Cruelty to Animals	To work for a world in which all humans respect and live in harmony with all other members of the	One of the goals of the RSPCA is to reduce the suffering of animals used in research by: challenging the necessity and	http://www.rspca.org.uk/

Name	Aim, vision, objective	Activities	Web link
(RSPCA), UK	animal kingdom.	justification for using animals; working to end substantial suffering in experiments; raising the welfare standards of laboratory animals worldwide; and ensuring UK standards are improved.	
Royal Society (UK)	Self-governing fellowship of the world's most distinguished scientists drawn from all areas of science, engineering, and medicine.	The Royal Society has published a guide for researchers about the use of non-human animals in research. The use of non-human animals in research: a guide for scientists (February 2004) has been produced by the Society's Animals in Research Committee.	https://royalsociety.org/
Home Office Animals in Science Regulation Unit (ASRU), UK	ASRU is a part of Home Office Science and is responsible for regulating the operation of the Animals (Scientific Procedures) Act 1986 (ASPAs)	ASRU regulates the use of animals in scientific research for the benefit of people, animals and the environment through the provision of impartial licensing procedures and evidence-based advice, and by encouraging the development and use of the 3Rs (Replacement, Reduction and Refinement) both nationally and internationally.	https://www.gov.uk/government/publications/animals-in-science-regulation-unit-annual-report-2013
Universities Federation for Animal Welfare (UFAW)	UFAW is an independent registered charity that works to develop and promote improvements in the welfare of all animals through scientific and educational activity worldwide	Promote and support developments in the science and technology that underpin advances in animal welfare; promote education in animal care and welfare; provide information, organises symposia, conferences and meetings, publishes books, videos, technical reports and the international quarterly scientific journal <i>Animal Welfare</i> ; provide expert advice to governments and other organisations and helps to draft and amend laws and guidelines etc.	http://www.ufaw.org.uk/
Huntingdon Life Sciences	Provide services for pharmaceutical, biopharmaceutical, agrochemical and chemical	Non-clinical, research services.	https://www.huntingdon.com/

Name	Aim, vision, objective	Activities	Web link
	companies, conducting developmental research to support global regulatory submissions.		
The Laboratory Animal Science Association (LASA)	The key aim of LASA is to advance this knowledge of the care and welfare of laboratory animals and to promote refinement of scientific procedures.	Continuing professional development; publication of position papers, reports, guiding principles, posters and other material; events; bursaries.	http://www.lasa.co.uk/about_lasa.html

Table 3: Overview of national organisations

7 Institutionalisation

As seen in section 5, a number of international, regional and national organisations are involved in encouraging ethical animal use principles and policies, use and promotion of alternative methods of animal testing, investigation and political lobbying on animal use in research, formulating policy and regulating animal use in research. In Europe, law, policy and institutional measures, as outlined, have worked towards institutionalising ethics assessment of the use of animals in research. As shown before, in Europe, Directive 2010/63/EU on the protection of animals used for scientific purposes⁶⁴ provides for detailed rules in order to eliminate disparities between laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes.

The European Union Reference Laboratory for Alternatives to Animal Testing (EURL-ECVAM), is hosted by the Joint Research Centre, Institute for Health and Consumer Protection (IHCP) located in Ispra, Italy.⁶⁵ The aim of EURL ECVAM is two-fold:

- To promote the scientific and regulatory acceptance of non-animal tests which are of importance to biomedical sciences, through research, test development and validation and the establishment of a specialised database service and
- To co-ordinate at the European level the independent evaluation of the relevance and reliability of tests for specific purposes, so that chemicals and products of various kinds, including medicines, vaccines, medical devices, cosmetics, household products and agricultural products, can be manufactured, transported and used more economically and more safely, whilst the current reliance on animal test procedures is progressively reduced.

Research laboratories are able to submit to EURL ECVAM for scientific validation the alternative methods to animal testing that they have developed. EURL ECVAM promotes the development and dissemination of alternative methods and approaches, their application in industry and their acceptance by regulators.

⁶⁴ European Parliament and of the Council, Directive 2010/63/EU on the protection of animals used for scientific purposes, 22 September 2010. <http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32010L0063>

⁶⁵ European Union Reference Laboratory for alternatives to animal testing (EURL-ECVAM). <https://eurl-ecvam.jrc.ec.europa.eu/>

The European Commission also collaborates with European trade associations, and companies from seven industry sectors in the European Partnership for Alternative Approaches to Animal Testing (EPAA) with the intention of pooling knowledge and resources to accelerate the development, validation and acceptance of alternative approaches to further the replacement, reduction and refinement (3Rs) of animal use in regulatory testing.

The H2020 and FP7 reference document ‘Ethics Review Checklist on Research on Animals’, which has been elaborated on the basis of Directive 2010/63/EU, stresses that:⁶⁶

Researchers should provide details of the species (and strains where appropriate) of animals to be used and explain why they have been chosen. They should explain why the anticipated benefits justify the use of animals and why methods avoiding the use of living animals cannot be used. They should also give details and justify the numbers of animals proposed with reference to statistical advice if applicable. They have to indicate what steps have been taken to comply with the principles of the 3 Rs: reduction, refinement and replacement. In particular, they should describe these procedures adopted to ensure that the amount of suffering to the animals is minimised and that their welfare is protected as far as possible (e.g. improvements in technique, application of humane end-points, environmental enrichment).

The checklist also states that when applying for authorisation by the competent national/local authority, the application must include at least the following:⁶⁷

- Relevance and justification of the (a) use of animals including their origin, estimated numbers, species and life stages and (b) procedures.
- Application of methods to replace, reduce and refine the use of animals in procedures.
- The planned use of anaesthesia, analgesia and other pain relieving methods.
- Reduction, avoidance and alleviation of any form of animal suffering, from birth to death where appropriate.
- Use of humane end-points.
- Experimental or observational strategy and statistical design to minimise animal numbers, pain, suffering, distress and environmental impact where appropriate.
- Reuse of animals and the accumulative effect thereof on the animals.
- The proposed severity classification of procedures.
- Avoidance of unjustified duplication of procedures where appropriate.
- Housing, husbandry and care conditions for the animals.
- Methods of killing.
- Competence of persons involved in the project.

It also requires that copies of the relevant authorisations are provided to the European Commission prior to the commencement of the research on animals.

In the UK

In May 2014, the ‘*Concordat on Openness in Animal Research*’ in the UK was launched; it currently has 85 signatories including universities, research councils, industry, non-profit

⁶⁶European Commission, “Research on Animals”.

http://ec.europa.eu/research/participants/data/ref/fp7/89837/research-animals_en.pdf

⁶⁷ Ibid.

organisations etc.⁶⁸ The Concordat commits its signatories to enhance their communication about their use of animals. Commitments include: being clear about when, how and why animals are used in research, enhancing communications with the media and the public about research using animals, being proactive in providing opportunities for the public to find out about research using animals and reporting on progress annually and sharing experiences.

8 International frameworks and protocols

This section looks at some international frameworks on the use of animals and animal welfare.

- **NASA Principles for Ethical Care and Use of Animals:**⁶⁹ stresses three principles particularly relevant to the ethics of research using animals: respect for life, societal benefit, and non-maleficence.
- **International Animal Welfare Agreement for Space Borne Research on the International Space Station:** establishes “a base line level of animal care and use in space that all countries could agree on”.⁷⁰
- **Universal Declaration on Animal Welfare (UDAW):**⁷¹ is a proposed inter-governmental agreement to recognise that animals are sentient, to prevent cruelty and reduce suffering, and to promote standards on the welfare of animals such as farm animals, companion animals, animals in scientific research, draught animals, wildlife and animals in recreation⁷²
- **International Guiding Principles for Biomedical Research Involving Animals,** Developed by the Council for International Organizations of Medical Sciences, Switzerland, 1985.
- **Guidelines for the welfare and use of animals in cancer research:** provide updated and enhanced recommendations for the care and use of animals in cancer research, to develop procedures that reduce, replace or refine animal studies and to communicate best practice throughout the world.⁷³ In all cases, however, the

⁶⁸ Understanding Animal Research, The Concordat on Openness in Animal Research in the UK. <http://www.understandinganimalresearch.org.uk/policy/concordat-on-openness-on-animal-research>

⁶⁹See NASA, NASA Principles for the Ethical Care and Use of Animals, 16 February 2001.

<http://www.nal.usda.gov/awic/pubs/IACUC/nasa.htm#pri>

⁷⁰Betancourt, Mark, “On the orbiting of species”, *Air & Space Magazine*

October 2011. <http://www.airspacemag.com/space/on-the-orbiting-of-species-111165162/#ixzz3lwcBGs00>

⁷¹ See World Animal Protection. <http://www.worldanimalprotection.org/take-action/back-universal-declaration-animal-welfare>

⁷² The UDAW was conceived in 2000 by a group of animal welfare organisations including World Animal Protection, (formerly the World Society for the Protection of Animals) which now acts as its Secretariat. It is supported by a planning group including Compassion in World Farming, Royal Society for the Prevention of Cruelty to Animals (RSPCA), the International Fund for Animal Welfare (IFAW) and the Humane Society of the United States. There have been several drafts of the declaration, with the most recent proposed in 2014. See Wikipedia. http://en.wikipedia.org/wiki/Universal_Declaration_on_Animal_Welfare

⁷³Workman, P., E.O. Aboagye, F. Balkwill, A. Balmain, G. Bruder, D. J. Chaplin, J. A Double, J. Everitt, D.A.H. Farningham, M. J. Glennie, L. R. Kelland, V. Robinson, I. J. Stratford, G. M. Tozer, S. Watson, S.R. Wedge, S.A. Eccles and an ad hoc committee of the National Cancer Research Institute, “Guidelines for the welfare and use of animals in cancer research”, *British Journal of Cancer*, 102, 2010, pp. 1555-1577.

Guidelines recommend that experimental designs and procedures should be tailored to the needs of the specific studies and are to be used in conjunction with appropriate national legislation.

- **Guide for the Care and Use of Laboratory Animals:** aims to “assist institutions in caring for and using animals in ways judged to be scientifically, technically, and humanely appropriate” and “assist investigators in fulfilling their obligation to plan and conduct animal experiments in accord with the highest scientific, humane, and ethical principles”.⁷⁴ The recommendations in the Guide are based on published data, scientific principles, expert opinion, and experience with methods and practices that have proved to be consistent with both high-quality research and humane animal care and use. The Guide is an internationally known reference document on animal care and use, and its use is required in the US by the Public Health Service Policy. Currently, it is in its eighth edition and over 550,000 copies have been printed since its first publication.

9 Other issues

Expansion of animal cloning to human cloning

One of the key ethical concerns of animal use in research and testing revolves around how cloning currently carried out only on animals might be extended to humans. This, it is said, would present technical difficulties based on the current state of the technology (“it would have to involve women willing to donate perhaps hundreds of eggs, surrogate pregnancies with high rates of miscarriage and stillbirth, and the possibility of premature ageing and high cancer rates for any children so produced”).⁷⁵ Whenever the issue of human cloning surfaces,⁷⁶ it generates ethical debates – for instance as occurred in 2004 when South Korean scientists announced they had cloned 30 human embryos, and in 2008 when scientists cloned mice from frozen tissue.⁷⁷ In principle, there is a moratorium on human reproductive cloning⁷⁸ (which has resulted in a lack of discussion on its ethical acceptability and implications) although researchers are still working on the subject.

⁷⁴ Committee for the Update of the Guide for the Care and Use of Laboratory Animals, Institute for Laboratory Animal Research, Division on Earth and Life Studies, National Research Council of the National Academies, Guide for the Care and Use of Laboratory Animals, The National Academies Press, Washington DC, Eighth Edition, 2011.

⁷⁵ Understanding Animal Research, “Animal Cloning”.

<http://www.understandinganimalresearch.org.uk/how/areas-of-research/animal-cloning/>

⁷⁶ See <http://www.unesco.org/new/en/social-and-human-sciences/themes/bioethics/international-bioethics-committee/ibc-sessions/eighteenth-session-baku-2011/human-cloning/>

⁷⁷ Ibid.

⁷⁸ See <http://www.unesco.org/new/en/social-and-human-sciences/themes/bioethics/international-bioethics-committee/ibc-sessions/eighteenth-session-baku-2011/human-cloning/>

10 Journal and conference series

Journals

- *Animal Welfare*: <http://www.ufaw.org.uk/animal.php>
- *ATLA, Alternatives to laboratory animals*: <http://altweb.jhsph.edu/pubs/journals/atla/>
- *Ethical theory and moral practice*: <http://www.springer.com/social+sciences/applied+ethics/journal/10677>
- *Journal of Agricultural and Environmental Ethics*: <http://www.springer.com/social+sciences/applied+ethics/journal/10806>
- *The ILAR Journal*: <http://ilarjournal.oxfordjournals.org/>
- *The Journal of Animal Ethics*: <http://www.press.uillinois.edu/journals/jane.html>

Conference series

- *Animal Replacement Science Conference*: <http://www.animalreplacementscience.com/>
- *Global Animal Law Conference*: <http://www.derechoanimal.info/esp/page/2988/welcome>
- *International animal rights conference*: <http://www.ar-conference.com/concept.php>
- *World Congress on Bioethics and Animal Rights*: <http://www.derechoanimal.info/eng/page/3387/iv-world-conference-on-bioethics-and-animal-rights>

11 Key publications

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3. Crettaz von Roten, F., “Public perceptions of animal experimentation across Europe”, *Public Underst. Sci.*, 22, 2013, pp. 691–703.
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9. House of Lords, *Select Committee on Animals in Scientific Procedures, Volume I—Report*, The Stationery Office, London, 2002.
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11. ICM, *Vivisection survey, conducted on behalf of BBC Newsnight*, ICM Research, London, 2006. <http://www.icmresearch.co.uk>
12. Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council, *Recognition and alleviation of pain and distress in laboratory animals*, National Academy Press, Washington, D.C., 2009.
13. Knight, Andrew, *The Costs and Benefits of Animal Experimentation*, Palgrave Macmillan, 2011.
14. Lilley, Elliot, Penny Hawkins, and Maggy Jennings, "A ‘Road Map ‘Toward Ending Severe Suffering of Animals Used in Research and Testing”, *Alternatives to laboratory animals: ATLA*, Vol. 42, No. 4, 2014, pp. 267-272.
15. Lund, Thomas Bøker, et al, “Painful dilemmas: A study of the way the public’s assessment of animal research balances costs to animals against human benefits,” *Public Understanding of Science*, Vol. 23, No. 4, 2014, pp. 428-444.
16. Matthiessen, L., B. Lucaroni, E. Sacherz, “Towards responsible animal research”, *EMBO Rep* 4, 2003, pp. 104–107.
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18. Pearson, Jeremy, "Use of animals in research and reporting of animal experiments-The need for improvement", *Vascular pharmacology*, Vol. 62, Issue 1, 2014, pp. 1-2.
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23. Webster, John, *Animal Welfare: Limping Towards Eden*, Wiley-Blackwell, 2008.