

Laboratory and Farm Animal Law

Opportunities for Ending Animal Use

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1. FROM FARM TO LABORATORY: COMPARING THE LEGISLATION

Directives set out general regulations applicable across the European Union; which Member States transpose into national law as appropriate. A number of Directives govern the use of animals by humans. Animals kept or bred for farming fall under *Directive 98/58/EC: Protection of Animals Kept for Farming Purposes* and the use of animals for research is regulated by *Directive 63/2010/EU: Protection of Animals Used for Scientific Purposes*.

Every year nearly 360 million pigs; sheep; goats and cattle as well as several billion poultry are killed in EU slaughterhouses. The European fur industry adds another 25 million animals to the figure. Hatcheries kill around 330 million day-old-chicks which are surplus to the egg industry. The control of contagious diseases may also require the killing of thousands to millions of animals (European Commission 2016).

Almost 11.5 million animals are used for research in the EU; including those for basic biological research; genetic modification experiments; toxicology testing and research and development of drugs (European Commission 2011). The most used species are mice; rats and fish; totalling around 10 million; as well as over 17.000 dogs; almost 4.000 cats and more than 6.000 primates (European Commission 2011). The economic value of livestock farming in the EU represents an annual value of €149 billion. The use of experimental animals is estimated to an annual value of €930 million (European Commission 2012).

The focus of both Directives is on the keeping animals for use by humans with the intention of promoting animal welfare. However; both

are led by economics; with Directive 98/58/EC aiming at “eliminating distortions of competition” (Council Directive 98/58/EC 1998) and Directive 2010/63/EU setting out to harmonise laboratory animal standards to reduce disparities between Member States which are “liable to constitute barriers to trade in products and substances” (Directive 63/2010/EU 2010).

Both Directives present conflicting ideals about the treatment of animals; by making statements on the importance of animal welfare; whilst setting standards for a life which inevitably involves suffering. Directive 98/58/EC states how animals shall not be kept unless it is “without detrimental effect on its health or welfare” (Council Directive 98/58/EC 1998). However; the minimum conditions for intensive factory farming is detrimental to health and welfare by nature; the routine use of antibiotics for example is a widespread practice to prevent the spread of disease (Landers et al. 2012). Directive 2010/63/EU affirms how animals “have an intrinsic value which must be respected” and recognises animals as “sentient creatures”; whilst licensing their use as tools in research which is known to cause pain; suffering and distress (Directive 63/2010/EU 2010).

One of the main differences between the laboratory and farm animal directives is how they perceive animal use. Directive 98/58/EC makes no comment on intrinsic value of animals; or any desire to put an end to the use of animals in food production (Council Directive 98/58/EC 1998). Directive 2010/63/EU however; acknowledges the use of animals in research to be ethically objectionable; noting the capacity of animals to feel pain; fear and distress whilst outlining a desire to end their use through the promotion and application of advanced scientific methodology; the 3Rs; specifically replacement (Directive 63/2010/EU 2010).

1.1. *The difference in perception allows a legislative move away from animal research*

This subtle but important difference in the spirit of Directive 2010/63/EU; allows for opportunities and potential for the eventual elimination of animal research; through a combination of review; assessment and implementation of non-animal methods. Recital 10 states:

While it is desirable to replace the use of live animals in procedures by other methods not entailing the use of live animals; the use of live animals continues to be necessary to protect human and animal health and the environment. However; this Directive represents an important step towards achieving *the final goal of full replacement of procedures on live animals for scientific and educational purposes* as soon as it is scientifically possible to do so. To that end; it seeks to facilitate and promote the advancement of alternative

approaches. It also seeks to ensure a high level of protection for animals that still need to be used in procedures. This Directive should be reviewed regularly in light of evolving science and animal-protection measures. (Directive 63/2010/EU 2010; emphasis added)

This encompasses the main tools available within the Directive for a phase out of animal testing: promotion and advancement of alternative methods; review of the legislation and consideration of scientific evolution; all legitimised by the final goal of full replacement of animals.

The principles of replacement; reduction and refinement are outlined in Article 4 of Directive 2010/63/EU. Member States are required to 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” (Directive 63/2010/EU 2010). Reduction and refinement (keeping the number of animal used in a procedure to a minimum and keeping pain; suffering or harm to animals to a minimum; respectively) are provisions which attend to animal welfare; but do not contribute to the aim of full replacement of animals in research.

Article 47 of Directive 2010/63/2010 stipulates further obligations for the Commission and Member States to “contribute to the development and validation of alternative approaches which could provide the same or higher levels of information as those obtained in procedures using animals” (Directive 63/2010/EU 2010); to set up laboratories for validation of alternative methods and ensure dissemination of these approaches.

2. RATIONALE FOR ENDING ANIMAL USE

The use of animals in scientific procedures with the intention of benefiting humans is fundamentally flawed due to “species differences”. Animal tests are an unreliable way to predict effects in humans because each species responds differently to substances. For example; penicillin is a useful antibiotic for people but it is lethal when tested in guinea pigs (Hamre et al. 1943). The breast cancer drug tamoxifen was designed as an oral contraceptive. It is in rats; but in women it has the opposite effect. It is now used in the treatment of breast cancer; despite causing cancer in rats in some studies (Read 1988). The cancer drug 6-azauridine can be used in humans for long periods; but in dogs small doses produce potentially lethal results in a few days (Weatherall 1982). Phenylbutazone works through the body slowly in humans; but in dogs it disappears in hours (Lees et al. 2004). The list of substances and their effects in different species is immeasurable.

Furthermore; the reliance on data from animals can produce unexpected adverse reactions in people in clinical trials; even fatal outcomes. TGN1412 – an experimental drug was given to human volunteers and caused life-threatening reactions; yet monkeys were given doses 500 times higher than the human volunteers and no side effects had been seen (Duff 2006).

Most recently; the French BIA 10-2474 drug trial; despite animal toxicity testing; went fatally wrong when given to human volunteers – one died; four showed evidence of brain damage (Callaway and Butler 2016). The substance had been tested on mice; rats; rabbits; dogs and monkeys for toxic effects on various organs as well as reproductive toxicity. Monkeys were given doses approx 75 times that given to the human volunteers (figures calculated from BIAL – Portela & Ca S.A. 2015; calculations available on request).

There are also ethical concerns held for animals used in research. The public are less accepting of the use of companion animals; such as dogs; cats and horses; as well as animals which are more like humans; such as monkeys. 75% of the UK public agree that more should be done to find alternatives to animals in research (Ipsos MORI 2016). In the political arena; there is also a strong desire to end the use of some of our closest relatives in research. 433 MEPs signed Written Declaration 40/2007 calling for a timetable to be set to end all experiments on non-human primates in Europe; at that time; the most supported Written Declaration on an animal protection issue ever (Animal Defenders International 2007).

Within various industries; non-animal technologies have been identified emerging areas with a potential to drive economic growth. This includes recognition of concerns about the predictivity of animal testing; acknowledgement of the scepticism of some researchers to move away from animal research; and the potential to improve safety and efficacy testing of chemicals and pharmaceuticals (Innovate UK 2015).

3. ADVANCING REPLACEMENT OF ANIMALS

Directive 63/2010/EU is progressive in that it includes provisions to advance the replacement of animals as described in Article 58:

The Commission shall review this Directive by 10 November 2017; *taking into account advancements in the development of alternative methods not entailing the use of animals*; in particular of non-human primates; and shall propose amendments; where appropriate. The Commission shall; where

appropriate; and in consultation with the Member States and stakeholders; conduct *periodic thematic reviews* of the replacement; reduction and refinement of the use of animals in procedures; paying specific attention to non-human primates; technological developments; and new scientific and animal-welfare knowledge. (Directive 63/2010/EU 2010; emphasis added)

The first paragraph recognises the need for legislation to be able to keep up with changes in science and pace of technological advancements. The thematic review; cited in the second paragraph; has the potential to provide a mechanism by which areas of animal research; or particular experiments; can be replaced with alternatives. But this must be effectively implemented by the Commission.

3.1. *Advancing thematic review*

The concept of thematic review provides a clear mechanism to keep pace with advances in technological and scientific progress; and move toward the ultimate goal of replacing animals in research. This can be achieved if the European Commission acts on Article 58 and implements a system of biennial thematic review; allowing relevant stakeholders to identify specific candidate areas of research for consideration and review.

The European Commission could coordinate Europe-wide activity; with Member States initiating projects. It is suggested that submissions relating to replacement of animals are prioritised over reduction or refinement; due to the former being able to contribute to the phasing out of animals use; the goal of this Directive. The process of conducting thematic review could be carried out using existing mechanisms for gathering data and scientific opinion; via a specific scientific committee. Proposals for the European Commission to carry out thematic review are as follows:

Step 1: Commission call for candidate submission

Following a call by the Commission; stakeholders should submit information on their rationale for proposed area of research for review; including referenced information such as:

- Area or method proposed for review.
- Estimates of number of animals involved and outline the typical procedures.
- An outline of the rationale for the proposal including; but not restricted to: available non-animal methods; evidence of unreliability of the model or lack of proven benefits or utility; severe suffering of animals with little or no demonstrable benefits; methods no longer used in certain countries; including outside the EU; consideration of evolving public opinion in particular research areas or using certain species.
- Identifying barriers and a demonstration of how these may be overcome.

Step 2: Candidate selection

The Commission should select a *minimum* of four candidates for replacement and one candidate for reduction or refinement to go forward for further review. The complexity and work required for each review may vary greatly from subject to subject; so the number of topics put forward for review may vary.

Step 3: In-depth review and research

The selected candidates would be given to a “Thematic Review Committee” for further review. For each candidate; the Committee will study each proposed aspect of the rationale for review; gather further information and make decisions on the potential steps towards replacement which can be made.

Ultimately this process would result in the publication of a report by the Thematic Review Committee with recommendations for each of the candidates; including proposals for establishing timetables for action.

Step 4: Report and establishment of timetables or dates for replacement/abandonment

Taking into account all of the information gathered over the course of the review; the Commission should establish a timetable of actions on each review topic. Depending on the status of the non-animal method; the nature of barriers and assessment of the actual value of the animal use; the timetable may span months or years; or may permit immediate implementation. The strategy may also include a number of courses of action; such as re-diverting funding; legislative changes or amendments and notifying Member States about the unacceptability of the particular use of animals.

4. THE IMPORTANCE OF ENDING ANIMAL USE

In comparison to Directive 98/58/EC; Directive 63/2010/EU has scope for making progress towards the goal of ending animal use in this area. Replacing the use of animals with alternative methods is important for reliable science; human health; economic reasons and because of ethical concerns which the public hold about subjecting animals to experiments. With the global recognition that animal agriculture is a major cause of ill health; early death and climate change; Directive 98/58/EC should emphasise plant food production and emulate the provisions included within Directive 63/2010/EU towards the final goal of ending animal use replacing animal food production with healthier plant options.

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