Animal Testing and the Regulation of Chemicals and Products: An RSPCA information paper

According to statistics published by the European Commission, 12 million animals were used in experiments in the EU in 2008.
Of these, 21.3% (2.6 million) were used in tests that were done to satisfy legal requirements.

Sixth Report on the Statistics on the Number of Animals Used for Experimental and other Scientific Purposes in the Member States of the European Union. COM(2010) 511 Final. Brussels 30.9.2010.


Photo: RSPCA photolibrary

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Introduction

Many types of product, ranging from pure chemicals used by industry to pesticides, medicines and foodstuffs, are subject to legal controls which include a requirement for an assessment of their safety. Manufacturers, suppliers or importers of products are obliged to provide the authorities with sufficient information to allow the regulators to assess the risks the products may pose to workers, consumers, or the environment. In some cases, the information must demonstrate that the product is effective for its intended purpose (efficacy), particularly in the case of medicines and vaccines. In many cases, the only type of information acceptable to the authorities is that derived from tests on animals. That is not to say that the law, as written, always explicitly says that safety tests must be done on animals, but in the majority of cases animal tests are considered necessary to satisfy their requirements.

In this information paper we explore some of the laws that lead to the use of animals for safety and efficacy testing, and to what extent this animal testing is dictated by the 'letter of the law' as opposed to its interpretation and implementation by regulatory authorities. An understanding of the nature and extent of legal requirements that result in animal testing is essential if ways are to be found to end animal use by changing the law, influencing the way it is implemented, or finding non-animal test methods that will satisfy the needs of achieving safety that underlie the relevant laws. Of course, laws vary throughout the world. In a global market, companies may have to satisfy a range of demands for testing if they are to sell goods abroad. However, this paper will concentrate on the laws applicable in the UK and the EU.

Warning! In the regulation of chemicals and products, nothing is simple. There are many types of product, many uses of chemicals, many differences between laws on different products, and many interpretations and opinions of what is needed to satisfy each law.

Acts, Regulations and Directives

In the UK, the basic laws (primary legislation) are Acts of Parliament. These are usually not very detailed, and the exact requirements for complying with each Act are spelled out in Regulations (secondary legislation pursuant to a particular Act). Increasingly, the UK is subject to laws made by the European Union. These laws take two forms - Regulations and Directives. EU Regulations are legally binding on all member states without modification, whereas Directives are addressed to the member state governments of the EU, and instruct them to implement the provisions of the Directive through their own national laws. This is usually done by amending regulations already issued under a UK Act, or issuing new regulations under the European Communities Act 1972.

The Acts of Parliament that underlie the control of chemicals and products do not define the type of test that must be done for safety assessment and therefore do not specifically mention animal testing. The more detailed UK Regulations sometimes do. It is common for new or amended UK Regulations to refer directly to parts of the relevant Directive. Many of the Directives that relate to the safety of products have annexes that define the specific information required and the tests that must be done, including tests on animals.

If someone tries to find exactly where in the law it says that an animal test must be done on a chemical or product, they will not find very much in the UK legislation (either Acts of Parliament or Regulations). They will usually have to follow the references in the UK Regulations to particular sections of an EU Directive, or read guidance documents produced by the regulatory authorities.

Technical Guidance and Guidelines

In many cases, even the EU Directives and Regulations are not detailed enough to cover all possible testing requirements for different types of product, or the different ways in which they are used. In an attempt to standardise the approach to testing, and to help manufacturers and suppliers comply with the law, a number of organisations provide detailed guidance on which tests should be done, and how the results should be interpreted. For example, the European Commission publishes Technical Guidance Documents on the testing requirements for biocides[1] and for the information requirements for compliance with EU chemicals legislation (REACH)[2].

For some products, the Directives and Regulations do not define the testing requirements at all, and simply include a legal requirement to ensure the safety of the product. How this is to be done is not explained. This is the case for example with cosmetics, where guidance was produced by the Scientific Committee on Cosmetic products and Non-Food Products intended for Consumers (now the Scientific Committee on Consumer Products)[3]. In fact, the use of animals to test cosmetics and their ingredients has been banned since 2009, rendering this guidance obsolete.

[1] Technical Guidance Document in support of Directive 98/8/EC concerning the placing of biocidal products on the market: Guidance on data requirements for active substances and biocidal products: http://ecb.jrc.ec.europa.eu/documents/Biocides/TECHNICAL_NOTES_FOR_GUIDANCE/TNsG_DATA_REQUIREMENTS/TNsG-Data-Requirements.pdf

[2] Guidance on Information Requirements and Chemical Safety Assessment (REACH): http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_en.htm?time=1292336611

[3] SCCNFP Notes of Guidance for the Testing of Cosmetic Ingredients and Their Safety Evaluation. SCCNFP/0690/03, 20 October 2003.

In most cases, a manufacturer or supplier may consult with a regulatory body (such as the UK Health and Safety Executive for chemicals, or the Medicines and Healthcare products Regulatory Agency for medicines) to obtain advice on the acceptability of particular tests. Although this advice would not be legally binding, it would clearly be in the manufacturer's interests to accept it.

Unfortunately, most EU Directives and guidance documents for the testing and risk assessment of chemicals and products require or advise the extensive use of tests on animals. There has been some progress on the refinement of these tests, and their replacement with non-animal test methods, but much more needs to be done before the pain, suffering and distress experienced by animals used in testing can be eliminated.

Standard test methods

The exact details of methods for testing the safety or effectiveness of products are rarely included in legal instruments. However, *Council Regulation No 440/2008 of 30 May 2008 laying down test methods pursuant to Regulation No 1907/2006 (REACH)* consists of a list of detailed protocols for testing chemicals, and may be cited by other Directives or Regulations. Most of the methods included are in fact reproduced from test guidelines published by the Organisation for Economic Cooperation and Development (OECD). For about 20 years, the OECD has been producing guidelines for safety testing which, through an agreement on the mutual acceptance of data, should be accepted as suitable for chemicals regulation in all OECD member countries. Many of these guidelines describe tests on animals, but they also provide a valuable focus for introducing non-animal test methods and animal welfare improvements to the existing methods.

Another important source of test methods is the European Pharmacopoeia, which produces monographs on the testing of many medicinal products, including vaccines and hormones (for quality control purposes). The use of these methods is mandatory under EU Directives controlling medicinal products. Unfortunately, many of these monographs describe animal tests for safety and effectiveness.

Whether animal tests are specified in primary or secondary legislation, recommended by official guidelines, or asked for by regulatory authorities, the manufacturers or suppliers of products know that they will be judged as being in breach of the law, or will not obtain authorisation for marketing the product, if they do not do them.

Survey of legal requirements for testing on animals

The following is a survey of some of the legal instruments that underlie the use of animals in the safety and efficacy testing of chemicals and products. The emphasis is on UK legislation, which in most cases implements EU legislation. It should be borne in mind that products intended to be sold outside the EU may also have to be tested on animals to conform with the legislation of non-EU countries.

Chemicals

Many chemicals used in industry, and in the household, are not covered by so-called 'sector-specific' legislation, that is to say they are not medicines, cosmetics, biocides and so on, which are controlled under specific laws. The way in which general chemicals are controlled within the EU was reorganised in 2007 with a ***Regulation for the Registration, Evaluation, Authorisation and Restriction of Chemicals*** **(REACH)**.

Under REACH, all substances (chemicals) placed on the EU market, or used in manufactured articles, must be registered with the European Chemicals Agency. Depending on the tonnage of each chemical put on the market, manufacturers, suppliers or importers must supply different amounts of information on the hazards associated with using their chemicals. This applies to both new substances and those which have been on the market for many years.

The results of animal tests are required for registration; the higher the tonnage marketed, the more animal testing is required. As a result of intense lobbying by RSPCA and other animal protection organisations, some flexibility was included in the REACH testing requirements, along with various measures such as compulsory sharing of information which will help limit animal testing. Although it is still too early to tell exactly how much animal testing will result from the implementation of REACH it is of great concern to the RSPCA[4].

The Health and Safety Executive (HSE), together with the Environment Agency, are responsible for administering REACH in the UK. As an EU Regulation, REACH does not need to be transposed into UK law, but enforcement of the REACH requirements is covered by the ***REACH Enforcement Regulations 2008*****.**

REACH supersedes the previous Dangerous Substances Directive[5] which was implemented in the UK by the Notification of New Substances Regulations 1993 (Pursuant to the Health and Safety at Work Act 1974). Requirements for the classification, packaging and labelling of chemicals, which were included in the Dangerous Substances Directive, and covered in the UK by the CHIP Regulations[6], will

[4] See *REACH - The new EU Chemicals Policy*: An RSPCA Information Paper.
[5] Council Directive 67/548/EEC of 27 June 1967 on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances, as amended.
[6] Chemicals (Hazard Information and Packaging for Supply) Regulations 2009

be replaced by a new EU Regulation[7]. However, these regulations do not generally require additional animal testing of individual chemical substances.

Mixtures of chemicals

Many products used in industry and the household contain a number of different chemicals mixed together e.g. paints, inks and cleaning materials. In general, the hazards of mixtures are assessed using existing information on individual chemicals, which in future will be provided largely through testing done for REACH. However, complying with the ***EU Regulation on the classification, packaging and labelling of substances and mixtures***[7] (and CHIP[6] In the UK) may require testing of a mixture. In most cases, it is not necessary to test the mixture itself, and animal testing is discouraged by the Regulations. In some cases, however, it may be thought necessary to test a mixture on animals if there is a possible interaction between the constituent chemicals, or where there is existing evidence of an adverse effect on human health.

Cosmetics

The basic EU legislation concerning cosmetic products is the **Cosmetics Directive (1976)**[8], which will be superseded during the next few years by the ***Cosmetics Regulation (2009)***[9]. The main requirement of the Directive is that *" A cosmetic product made available on the market shall be safe for human health when used under normal or reasonably foreseeable conditions of use..".* There are no explicit requirements for testing new products or ingredients, and the way in which the safety of a new cosmetic product is assessed is the responsibility of the manufacturer or supplier. However, guidance has been produced by the Scientific Committee on Cosmetic products and Non-Food Products intended for Consumers (see footnote 3) and this recommends the use of animal tests for a number of types of toxicity.

The RSPCA campaigned for many years against the use of animals to test cosmetics. An end to the animal testing of cosmetics (and ingredients) in the UK was obtained in 1998. Prohibition of the testing on animals of cosmetics and their ingredients in the whole EU, and the marketing of animal-tested cosmetics, was introduced in an amendment to the Cosmetics Directive in 2003[10], phased in over a period of nine years. In the UK, these bans are implemented by the ***Cosmetic Products (Safety) Regulations 2008***, (under the Consumer Protection Act 1987).

[7] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures.
[8] Council Directive 76/768/EEC of 27 July 1976 on the approximation of the laws of the Member States relating to cosmetic products: Directive 2003/15/EC, the 7th Amendment.
[9] Regulation (EC) no 1223/2009 of the European Parliament and of the Council of 30 November 2009 on Cosmetic Products (recast)
[10] Directive 2003/15/EC; the 7th Amendment to the Cosmetics Directive.

It must be remembered that cosmetics and their ingredients may be subject to controls other than the Cosmetics Directive/Regulation. New ingredients, if they are chemical substances, will be subject to notification as general chemicals, and may be tested on animals as a way of assessing the safety of workers who produce the chemical, or use it in cosmetics manufacture. In some cases, ingredients may have properties that make them liable to be treated as biocides or pharmaceuticals, in which case more testing may be demanded.

Household products

Many products used in the household (such as cleaners, fly-spray or air fresheners) will contain a mixture of chemicals. As mixtures, there should be no demand for animal testing of the finished product. However, the individual ingredients may be subject to various legal requirements, such as those for general chemicals, pesticides, or biocides. In fact, very few ingredients of household products are 'new' or used in no other type of product, for example for industrial or agricultural use.

Human medicines and medical devices

Directive 2001/83/EC[11] lays down the basic rules for the control of human medicines in the EU. No medicinal product may be placed on the market without a marketing authorisation, and to obtain this, the applicant must supply a great deal of information to the authorities. This includes most of the standard toxicological tests, some on both a rodent and a non-rodent species. In addition, there are requirements for demonstrating that the medicine works as intended, which may also involve animal testing. For details of the test methods to be used, the Directive refers to guidance from the European Medicines Agency (EMA), which is the central medicines authority for the EU. The guidelines issued by the EMA leave no doubt that animal testing will be regarded as essential for the licensing of most medicines. Some of the guidelines reproduce those of the **International Conference on Harmonisation** (ICH) which has been working to reach agreement worldwide on the methods used to test new medicines. ICH has had a very beneficial effect by reducing the need to do each animal test in several different ways, to satisfy regulators in different countries. It also forms an effective focus for introducing measures to refine the methods used.

For a variety of medicinal products such as vaccines and hormones, where individual batch testing is often required, testing must be done according to **European Pharmacopoeia monographs**. Directive 2001/83/EC says that for control tests on

[11] Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use.

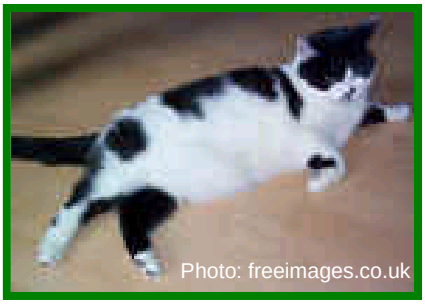
finished products, *"The provisions of the monographs for pharmaceutical forms, immunosera, vaccines and radiopharmaceutical preparations of the European Pharmacopoeia ..... shall be applicable to all products defined therein."* Many monographs specify tests on animals, and large numbers of animals are used every year to test new batches of products such as tetanus and diphtheria vaccine.

In the UK, the Directive is implemented by Regulations such as ***The Medicines for Human Use (Marketing Authorisations etc.) 1994 Regulations*** and ***The Medicines (Codification Amendments etc.) Regulations 2002***, both of which are pursuant to the Medicines Act 1968. With regard to testing requirements, these laws simply refer to the 'relevant community provisions', which in effect means the Directive.

In this country, the Medicines and Healthcare products Regulatory Agency (MHRA) is responsible for licensing medicines for use in humans, and in EU terms is the 'UK Competent Authority'.

Medical devices (any instrument, apparatus, appliance, material or other article used in diagnosis, prevention, monitoring, treatment or alleviation of disease), are regulated by ***EU Directives 90/385/EEC, 93/42/EEC, and 98/79/EC***[12]. These are implemented in the UK by ***The Medical Devices Regulations 2002*** (Consumer Protection Act 1987), administered by the MHRA. The methods to be used for safety testing are not specified in the Directives or UK Regulations, but are issued as international standards (ISO)[13]. ISO is a network of the national standards institutes of 153 countries, with a central secretariat in Geneva, Switzerland. The ISO standards for the biological evaluation of medical devices include a number of tests on animals. The MHRA has issued guidance on safety evaluation, which describes a flexible process based on the ISO standards[14].

Veterinary medicines



Veterinary drugs are regulated in a similar way to medicines for human use. The testing that is required for marketing authorisation is described in the EU ***Directive 2001/82/EC***[15] and guidance is given in *The rules governing medicinal products in the European Union, Volume V - Pharmaceutical Legislation, Veterinary Medicinal Products*. Animal testing is required, but for some tests the animal species for which the medicine is intended may be used as the second species, after tests in rodents. The testing requirements are more extensive, and involve more animal use, if the medicine is intended for food-producing animals, since safe levels must be set

[12] Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices; Council Directive 93/42/EEC of 14 June 1993 concerning medical devices; Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices.
[13] BS EN ISO 10993 1-17 Biological Evaluation of Medical Devices
[14] EC Medical Devices Directives: guidance on the biological safety assessment (MHRA)
[15] Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products.

for veterinary residues in the food. Animals are also used in trials which are the animal equivalent of human clinical trials. Quality control tests on products such as vaccines are described in European Pharmacopoeia monographs, as for human medicines.

In the UK, the Directive is implemented by the ***The Veterinary Medicines Regulations 2009*** (issued under the European Communities Act 1972), which is administered by the Veterinary Medicines Directorate of DEFRA.

Pesticides


Photo: freeimages.co.uk

EU law recognises two types of 'pesticide'
- **plant protection products**, intended to protect plants or plant products against harmful organisms. This includes insecticides, fungicides and herbicides. They require authorisation before they can be marketed or used, and are regulated by the ***Plant Protection Products Directive***[16] *(to be replaced by Regulation (EC) 1107/2009),* implemented in the UK by a number of Regulations[17].

- **biocides** are defined as *products intended to destroy, deter, render harmless, prevent the action of, or otherwise exert a controlling effect on any harmful organism*. They include products such as disinfectants, rodenticides and wood preservatives. They also require authorisation before they can be marketed or used, and are regulated by the ***Biocides Directive***[18]**,** implemented in the UK by the ***Biocidal Products Regulations 2001***.

Both Directives include requirements for many tests on animals, although the testing requirements in both Directives are currently under revision. The Chemicals Regulation Directorate of the HSE is responsible, along with DEFRA, for enforcing the UK regulations. Advice on testing and risk assessment for biocides is given by the European Commission in its Technical Guidance Document (see footnote 1).

Food

Food Additives: Many chemicals may be added to food, for a variety of reasons. Additives may be colours, preservatives, anti-oxidants, emulsifiers, thickeners, stabilisers, acidity regulators, sweeteners or firming agents. There is a basic 'framework' EU Directive relating to food additives[19], but also separate Directives on

[16] Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market.
[17] The Control of Pesticides Regulations 1986, pursuant to the Food and Environment protection Act 1985; The Plant Protection Products Regulations 2005, pursuant to the European Communities Act 1972.
[18] Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing of biocidal products on the market.
[19] Council Directive 89/107/EC of 21 December 1988 on the approximation of laws of the Member States concerning food additives authorised for use in foodstuffs intended for human consumption; European Parliament and Council Directive 95/2/EC 20 February 1995 on food additives other than colours and sweeteners, as amended by Directives 96/85/EC, 98/72/EC and 2001/5/EC.

flavours, sweeteners and colours. These are implemented by an equally extensive series of UK regulations under the Food Safety Act 1990.

No additive may be used unless it satisfies the requirements of Annex II of the framework Directive, one of which is that it must present no hazard to the health of the consumer. Part of the process of approval is a safety evaluation by the EU Scientific Committee on Food, and the SCF has published guidance on what testing is required[20]. This includes a large array of animal tests.

Food supplements, such as concentrated vitamin and mineral tablets, multivitamins and herbal extracts (non-medicinal) are controlled by *EU Directive 2002/46/EC*[21] and in the UK by the Food Supplements Regulations 2003. The competent authority for the EU is the European Food Safety Agency, and in the UK it is the Food Standards Agency. Guidance on the safety evaluation of food supplements has been published by the Scientific Committee on Foodstuffs[22]. At present, there seems to be little justification for animal testing of supplements, although there is a danger that tests will be requested by the authorities on some products.

Food contact materials, such as plastic wrappings, come under *EU Directives 89/109/EEC and 2002/72/EC*, implemented in the UK by *the Materials and Articles in Contact with Food Regulations 1987* and the *Plastic Materials and Articles in Contact with Food Regulations 1998*. The Scientific Committee for Food has produced guidance on the testing required for substances used in these products[23], and some animal testing is included.

Shellfish are routinely tested on animals. Under *EU Directive 91/492/EEC*[24], the standard method for testing shellfish for the presence of algal toxins is the mouse 'bioassay' in which samples derived from shellfish are injected into mice to see if they cause death. Shellfish beds are monitored regularly, and large numbers of mice are used each year. The UK legislation is *the Food Safety (Fishery Products and Live Shellfish) (Hygiene) Regulations 1998*, administered by the Food Standards Agency. Alternative tests, based on chemical detection of toxins, have now been validated and will replace the animal tests in the near future.

[20] Guidance on submissions for food additive evaluations by the scientific committee on food (2001)
[21] Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of Member States relating to food supplements.
[22] Guidance on submissions for safety evaluation of sources of nutrients or of other ingredients proposed for use in the manufacture of foods: SCF/CS/ADD/NUT/21 Final 12 July 2001
[23] SCF/CS/PLEN/GEN/100 Final 19 December 2001,Guidelines of the Scientific Committee on Food for the presentation of an application for safety assessment of a substance to be used in food contact materials prior to its authorisation.
[24] Directive 91/492/EEC of 15 July 1991 laying down the health conditions for the production and placing on the market of live bivalve molluscs.