

Homeopathy and animal testing

The legal position in the European Union



David Thomas is a UK solicitor. He has been legal consultant to several animal protection and human rights NGOs, including Cruelty Free International, and has brought numerous test cases in the UK and Europe. Formerly a litigation partner in a West End firm, he is a consultant to Bindmans LLP and was legal officer to Child Poverty Action Group. He has written numerous articles about legal and related issues and contributed to a number of books. He has taught judicial review and human rights law and is a part-time judge.

by David Thomas

Where no claim about specific therapeutic indication is made on the label or elsewhere, homeopathic medicines do not have to be authorised by medicines regulators in the European Union (EU): a simplified registration procedure can be followed instead, without the extensive data required for authorisation. This is largely because homeopathic medicines are considered safe.

In this context, it is difficult to see how animal research to test the efficacy of homeopathic medicines can be lawful under EU law. It fails key legal tests: the alternatives test and the harm:benefit test.

The article ‘Doing harm in homeopathy: seven good reasons why we should not experiment on animals’ by Delny Britton (*HIP* Autumn / Winter 2014, page 18) does just what it says on the tin: Dr Britton argues the case against experimenting on animals as a method of establishing the efficacy of homeopathic products.

Given its philosophy as a gentle form of medicine, working with an individual’s body and mind rather than the antagonistic, even brutal, way in which allopathic medicine is often used, it will come as a surprise to many – it certainly came as a surprise to me – that in some countries animals are used to test homeopathic products. From Dr Britton’s description of certain experiments, the suffering visited on animals can be every bit as high as that involved in testing conventional medicines.

The question is whether the use of animals for this purpose is legal. Dr Britton touches on this and I will expand on the issues in this article. I will consider the position in the EU. Because homeopathic medicines are generally considered safe, testing on animals appears to be focussed on efficacy rather than toxicity.

I will first explain how homeopathic medicines are regulated under EU medicines law and then consider how EU law dealing with animal experiments should be applied to such products.

Regulation of homeopathic medicines

Homeopathic medicines intended for human use are, like allopathic ones, regulated under Directive 2001/83/EC (the medicines directive). Medicines, homeopathic and

allopathic, intended for animal use are regulated under Directive 2001/82/EC (known as the veterinary medicines directive). The two directives contain similar rules for homeopathic medicines; I will focus on the human variety.

Article 1(5) of the medicines directive defines ‘homeopathic medicinal product’ as:

Any medicinal product prepared from substances called homeopathic stocks in accordance with a homeopathic manufacturing procedure described by the European Pharmacopoeia or, in the absence thereof, by the pharmacopoeias currently used officially in the Member States. A homeopathic medicinal product may contain a number of principles.

Homeopathic medicines are given special treatment by the medicines directive. Instead of the authorisation which allopathic medicines must obtain from a regulator, they can normally simply be registered. An applicant for authorisation has to supply extensive data on safety, efficacy and quality, amongst other things.

Recital (21) explains the reason for the special treatment:

Having regard to the particular characteristics of these homeopathic medicinal products, such as the very low level of active principles they contain and the difficulty of applying to them the conventional statistical methods relating to clinical trials, it



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is desirable to provide a special, simplified registration procedure for those homeopathic medicinal products which are placed on the market without therapeutic indications in a pharmaceutical form and dosage which do not present a risk for the patient.

So, the key factors are no risk to patients and the absence of therapeutic indication: to avoid the need for authorisation, the manufacturer of a homeopathic medicine cannot claim (and, indeed, usually does not want to claim, given the way homeopathic medicines are prescribed): 'use this product to cure disease x'.

Recital (22) then says that anthroposophic medicinal products described in an official pharmacopoeia and prepared by the homeopathic method are to be treated like homeopathic medicines. Anthroposophic medicines share some characteristics with homeopathic ones, such as ultra-dilution of a substance.

Articles 14 and 15 enact the simplified registration procedure foreseen by recital (21). The option

applies to homeopathic medicines manufactured or marketed in the EU.

There are three conditions set out in Article 14 which must be satisfied before registration – rather than authorisation – is permitted:

- The medicine must be administered orally or externally.
- There must be no claim of specific therapeutic indication on a label or elsewhere.
- There must be sufficient dilution to guarantee safety. In

'Forced swim test' cylinders

particular, the product ...

... may not contain either more than one part per 10,000 of the mother tincture or more than 1/100th of the smallest dose used in allopathy with regard to active substances whose presence in an allopathic medicinal product results in the obligation to submit a doctor's prescription.

The European Commission is given the power to amend the third criterion if new scientific evidence warrants it, but has not done so.

The simplified registration procedure may, under Article 15, cover a series of medicines derived from the same homeopathic stock, provided pharmaceutical quality and batch-to-batch homogeneity is shown.

A number of documents must accompany the application for registration, including: a dossier describing how the homeopathic stock is obtained and controlled; a manufacturing and control file for each pharmaceutical form with a description of the method of dilution and potentiation; and data relating to the stability of a medicine. These are essentially quality control measures. ➤

The forced swim test leads to considerable suffering and is indeed designed to

➤ Article 14(3) says that various rules in the directive applying to allopathic medicines – such as information about controls – apply by way of analogy to homeopathic medicines (although it is difficult to see how some of them could apply, given that there is no need for authorisation). The mutual recognition rules – whereby registration or authorisation in one member state generally entitles the manufacturer to registration or authorisation in other member states – apply to homeopathic medicines as much as to allopathic ones (Article 13(1)). However, the pharmacovigilance rules set out in Title IX do not apply to registered homeopathic medicines. Pharmacovigilance involves monitoring the safety of medicines used in clinical practice. Again, the exemption is presumably because homeopathic medicines are considered safe.

Article 16 is important. Homeopathic medicines which do not comply with Article 14 – for example, because a therapeutic indication is claimed – have to be authorised and labelled in the same way as allopathic medicines.

Para (2) then says:

A Member State may introduce or retain in its territory specific rules for the preclinical tests and clinical trials of homeopathic medicinal products other than those referred to in Article 14(1) in accordance with the principles and characteristics of homeopathy as practised in that Member State.

So, a member state can, for homeopathic medicines, supplement – and, perhaps (it is not clear), supplant – the requirements for allopathic medicines under the directive where (for example) a therapeutic indication is claimed. The additional requirements can extend to preclinical tests, which include animal tests. I understand that, from January 2016, in Italy homeopathic medicines will need a safety dossier, albeit a simplified one compared with allopathic medicines. Italy is home to some animal tests involving homeopathic medicines.

The position in the UK

It is for individual member states to establish the details of the registration procedure they will operate. In the UK, the relevant agency is the Medicines and Healthcare

products Regulatory Agency (MHRA) for human homeopathic medicines and the Veterinary Medicines Directorate for animal homeopathic medicines. These two agencies also regulate allopathic medicines.

The MHRA also operates a national rules scheme, which shares some features of both registration and authorisation. The scheme allows a manufacturer to claim that a product is used within the homeopathic tradition for the relief or treatment of minor symptoms and conditions not requiring the supervision of a doctor. Whereas under the simplified registration procedure an applicant need only provide data demonstrating quality along with dilution of such a degree that safety can be assumed, under the national rules scheme data demonstrating quality, safety and use within the UK homeopathic tradition must be provided, as well as product literature and information about labelling. It is not clear whether the MHRA has introduced the scheme under the power given by Article 16(2) of the medicines directive.

The animal experiments directive

In the EU, animal experiments are governed by Directive 2010/63/EU (the animal experiments directive).

There needs to be a legal challenge to experiments on animals

This replaced a 1986 law (Directive 86/609/EEC). The 28 member states have had to introduce the provisions of the directive into their national legislation, for most purposes from 1 January 2013. In the UK, for example, extensive amendments were made to the Animals (Scientific Procedures) Act 1986 (ASPA) to bring it into line with the directive.

The directive requires prior authorisation by member states before a programme of animal experiments may take place. There are many aspects to this but, in the present context, there are two key tests someone wishing to experiment on animals must meet in order to obtain authorisation:

- **The alternatives test:** this is often known as the Three Rs principle (replacement, reduction and refinement): animal experiments may not be carried out when the desired scientific information could be obtained without using animals (replacement), by using fewer than proposed (reduction) or by causing less suffering than proposed (refinement).
- **The harm/benefit test:** before a member state may grant authorisation for an animal experiment, it must weigh the likely harm to the animals against the likely benefit – to humankind, other animals or the



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environment. Only if the benefit outweighs the harm may authorisation be granted.

The two tests are cumulative – both must be satisfied before authorisation for an animal experiment may be granted. I will address each in turn.

Alternatives test

Article 4 of the animal experiments directive provides:

1. 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.
2. Member States shall ensure that the number of animals used in projects is reduced to a minimum without compromising the objectives of the project.
3. 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.
4. This Article shall, in the choice of methods, be implemented in accordance with Article 13.

So, paragraphs (1), (2) and (3) enact, respectively, the replacement, reduction and refinement principles. Article 4 is reflected in section 2A of ASPA.

Article 13(1) of the animal experiments directive then deals with regulatory toxicity testing:

Without prejudice to national legislation prohibiting certain types of methods, Member States shall ensure that a procedure is not carried out if another method or testing strategy for obtaining the result sought, not entailing the use of a live animal, is recognised under the legislation of the Union.

The introductory phrase ‘Without prejudice to national legislation prohibiting certain types of methods’ allows member states to prohibit what would otherwise be an animal replacement method. An example is research on human embryos, prohibited in many Catholic member states. Where a member state has such a law, one could not argue that the method constitutes an available replacement to the animal method. Paragraphs (2) and (3) of Article 13 then reinforce the reduction and refinement limbs of the Three Rs principle.

I can see no reason why testing a homeopathic medicine on humans cannot, in principle, constitute an alternative strategy

So, Articles 4(1) and 13(1) talk about *testing strategies* not involving animals, not simply *non-animal methods*. It is, therefore, not necessary to identify a particular technique not using animals which can directly replace an animal technique. If the same scientific objective can be achieved, it does not

In some countries animals are used to test homeopathic products

matter that the approach may be wholly different from that involved for the animal method. It may, for example, be multi-step or involve the analysis of existing data, on the same or a related product.

Or it may involve testing on human beings. I can see no reason why testing a homeopathic medicine on humans cannot, in principle, constitute an alternative strategy. This is subject to the important proviso that international ethical norms, including the obtaining of properly informed consent, are met. The leading international instrument governing research involving humans is the *Declaration of Helsinki* (the declaration), last updated in October 2013 (wma.net). This covers both safety and efficacy testing on volunteers as well as patients. There is nothing in the declaration which would represent an obstacle to giving homeopathic medicines to informed and consenting volunteers or patients in a trial – precisely because the medicines are considered not to present any safety concerns. In terms of risk, homeopathic medicines can be seen as the >



➤ equivalent of placebos – indeed, that is also the criticism often made by conventional practitioners about homeopathic medicines from the point of view of efficacy.

The harm:benefit evaluation

Articles 36 and 38 of the animal experiments directive provide:

Article 36:

2. Member States shall ensure that no project is carried out unless a favourable project evaluation by the competent authority has been received in accordance with Article 38.

Article 38:

1. The project evaluation shall be performed with a degree of detail appropriate for the type of project and shall verify that the project meets the following criteria:
 - (a) the project is justified from a scientific or educational point of view or required by law
 - (b) the purposes of the project justify the use of animals; and
 - (c) the project is designed so as to enable procedures to be carried out in the most humane and environmentally sensitive manner possible.
2. The project evaluation shall consist in particular of the following:
 - (a) an evaluation of the objectives of the project, the predicted scientific benefits or educational value
 - (b) an assessment of the compliance of the project with the requirement of replacement, reduction and refinement
 - (c) an assessment and assignment of the classification of the severity of procedures
 - (d) a harm:benefit analysis of the project, to assess whether the harm to the animals in terms of suffering, pain and distress is justified by the expected outcome taking into account ethical considerations, and may ultimately benefit human beings, animals or the environment.

In addition to meeting the alternatives tests, a researcher proposing to test a homeopathic medicine on animals would therefore need to demonstrate that (i) the experiment is likely to lead to benefit (identifying it) and (ii) the anticipated benefit will outweigh the suffering likely to be experienced by the animals.

Not all types of benefit can be taken into account. Under Article 38(1), the project must (i) be justified from a scientific or educational point of view or (ii) required by

law. A desire on the part of the researcher to advance his or her career or secure grant funding, or a wish by a company to make money, are not legitimate benefits.

Similarly, the mere fact that new knowledge will be gained is not sufficient. Under Article 5 of the directive, basic (or fundamental) research is a permissible purpose of an animal experiment, but it is still necessary to identify a practical benefit, even if it is not immediate.

Nor, in my view, is it legitimate to generate data which, it is hoped, will be useful in the propaganda war between proponents and opponents of homeopathy, by demonstrating the efficacy of particular medicines in laboratory animals. Benefit has to be more

specific than that and related directly to human health, the health of other animals (i.e. not those experimented upon) or the environment.

In her article, Dr Britton identifies three reasons for conducting homeopathic research (not just that involving animals): to increase the evidence base; to determine mode of action; and to improve clinical care of patients. These are clearly interrelated and ultimately collapse into the third objective. Dr Britton argues convincingly why animal research does not meet these objectives: mode of action can as easily be studied in human patients, human tissue, plants etc (and testing on animals for this purpose therefore breaches the alternatives

principle); homeopathic animal research uses an approach borrowed from allopathic research but the principles of homeopathy are very different – for example, it does not subscribe to the ‘one size fits all’ or ‘one condition one remedy’ philosophies and is individualised for each patient; homeopathy is a form of energy medicine (which allopathic medicine is not); it looks at emotional states (which allopathic medicine usually does not); and it is holistic, not reductionist like its allopathic counterpart.

Karin Mont makes similar points in her article ‘Desperate Measures’ (*HIP* Summer 2015, page 4). These seem to me to be powerful objections. Performing tests on animals undoubtedly increases the evidence base, but are the results *useful*? Ultimately, the question is: what benefit, in the real world, could realistically be obtained from conducting the proposed animal experiment on a homeopathic medicine? Unlike with allopathic medicines, it cannot be argued that the data is needed to obtain authorisation, so that cannot be a benefit in itself.

There can only be benefit, it seems to me, if the data from animal experiments would be useful for homeopathic practitioners in deciding what to prescribe. For all the reasons discussed in Dr Britton’s article, it seems highly unlikely that the data would be useful for practitioners.

An example

Take one of the research projects mentioned by Dr Britton. This was conducted by Sandra Pinto et al in Brazil (2008). Their research paper in fact describes two experiments, designed to assess the ability of *Chamomilla*, a homeopathic medicine, to reduce stress: in other words, the experiments were assessing the efficacy of *Chamomilla*. In the first, half the mice were given a highly malignant tumour and paired in cages with healthy mice. These mice were either given 10% ethanol (a vehicle used in homeopathic preparations) or *Chamomilla*. A third subgroup (the baseline control) received no treatment and did not cohabit with tumour-bearing mice. It appears that the hypothesis was that simply cohabiting with a tumour-bearing mouse could cause healthy mice stress, and the objective was to ascertain how ethanol

Homeopathic research involving animals seems not to take place in the UK

and *Chamomilla* fared in reducing the stress compared to the baseline control animals (stress being measured by locomotion, rearing, defecation and grooming).

The second experiment involved the notorious 'forced swim test', where animals are placed in narrow cylinders filled with water, forcing them to swim continually to avoid drowning. It is designed to assess stress; the theory is that, the sooner an animal stops swimming, the more depressed it is. Each of four groups of mice was subjected to the swim test: one group was treated with water (the baseline control), another with 10% ethanol, another with *Chamomilla* and the fourth with water and amitriptyline (an anti-depressant drug).

The authors concluded:

In both models, mice treated with *Chamomilla* 6cH partly recovered the baseline control patterns. This partial recovery effect suggests that a putative adaptation behaviour may be attributed to the *Chamomilla* 6cH treated mice; i.e. these animals would have a tendency to revert more quickly to the 'normality state', after being subjected to a stressful condition.

In the forced swim test, amitriptyline- and ethanol-treated animals fared better than the *Chamomilla*-treated mice on the stress indicators but the *Chamomilla*-treated mice did better than the baseline control mice.

The studies may, perhaps, be of some scientific interest. But the crucial question is: of what benefit are the results in the real world? Would any homeopathic practitioner decide to prescribe *Chamomilla* (or amitriptyline or ethanol) for an individual patient experiencing stress – *because of* these results? It seems extremely unlikely, given the principles underpinning homeopathy.

This was a Brazilian homeopathy study, claimed by the authors to be legal under the laws of that country. The equivalent study could not be permitted in the EU, unless a potential practical benefit could, contrary to appearance, be identified.

Even then, the benefit would have to be weighed against the suffering of the animals. The authors do not describe the symptoms of the tumour-bearing mice, although they noted that many tumours grew exponentially. These mice must, in fact, have suffered significantly. The other mice had blood taken by cardiac puncture under



Homeopathy does not take a 'one size fits all' approach

general anaesthesia, with all that that involves. The forced swim test, too, leads to considerable suffering and is indeed designed to. Under the animal experiments directive, forced swim or exercise tests causes are considered 'severe' where exhaustion is the end-point (which it may not have been here).

Because the suffering must have been considerable, potential benefit would need to be correspondingly significant to justify grant of authorisation.

Homeopathic research involving animals seems not to take place in the UK. Given the fact that over four million animals are used in experiments in the UK every year, and the benefit to be gained from some appears speculative or slight at best, this may provide eloquent testimony to the difficulty of identifying legitimate benefits from homeopathic animal research.

There needs to be far greater scrutiny of, and perhaps legal challenge to, experiments on animals

Conclusion

The alternatives and harm:benefit tests have to be applied on a case-by-case basis. It is not possible to say in the abstract that they could *never* be met when testing the efficacy of homeopathic medicines. It is possible to say, however, that it is very difficult to see how they could be met, given the scientific theory underlying homeopathy, the wealth of experience garnered over two centuries with human patients and the ethical availability of such patients, who are likely to provide an immeasurably better guide to the effectiveness of a homeopathic medicine than stressed laboratory animals used in artificial experiments adopting an approach foreign to homeopathy.

Outside the EU, there may not always be the same legal constraints. The regulation of homeopathic medicine varies considerably around the world. However, institutional ethical input is often required, even if not mandated by the law. That should lead to the same evaluation of harm and benefit and the availability of alternatives (including human patients in ethical studies).

It seems to me that, within the EU, there needs to be far greater scrutiny of, and perhaps legal challenge to, experiments on animals to test the efficacy of homeopathic medicines, on the basis that they do not meet the harm:benefit and alternatives tests under the animal experiments directive.

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David Thomas can be contacted at david.thomas@crueltyfreeinternational.org. □