EUROPEAN COALITION TO END ANIMAL EXPERIMENTS

testing TIMES

Monthly Update on Animal Experimentation Issues in the EU from the ECEAE

ISSUE No. 5: September 2006

Welcome to the September edition of Testing Times.

The main focus this autumn is the Second Reading of the REACH chemicals legislation due for vote in the European Parliament in November and the Council in December. There is still an enormous amount at stake and the lives of many millions of animals will be decided over the next four months.

The ECEAE Annual General Meeting will take place in October. It is being held in Helsinki, continuing the tradition of following the Presidency of the European Union. Helsinki will also be the home of the European Chemicals Agency due to open next year.

This month we welcomed a new member, Svoboda Zvířat from the Czech Republic, to the Coalition. Although one of our smaller members, they are a dynamic and passionate group who gave an impressive presentation at our last meeting. We are confident that they will prove a valuable member.

I hope you enjoy this edition of Testing Times. If you have any questions regarding laboratory animal issues in the EU, please feel free to contact me.

Warm regards,

Sandra Hannen,
European Policy Director, ECEAE

This Issue

REACH nears Second Reading

This autumn will finally see the Second Reading of the REACH chemicals legislation. The deadline for MEPs to submit amendments on the Environment Committee was 11th September. The latest schedule has the Environment Committee vote taking place on 10th October, the Parliament vote on 14th November and the Council vote following on 4th December.

There are many amendments aimed at reducing the use of animal testing that were passed by the Parliament in their First Reading but which were subsequently removed by Council. If the legislators are going to respect their commitment to reducing animal experimentation then certain amendments must be passed in Second Reading.

In particular, amendments to the following effect must be included:

- The Parliament's First Reading solution to keeping cosmetics products out of the legislation is superior to the Council's and should be re-instated.
- There must be a Committee for Alternative Test Methods within the Chemical Agency to ensure the quick uptake and use of alternatives.

- Part of the registration fee should be used for the development of alternative tests.
- Dossier submissions must include information on animal tests and the numbers of animals used.
- ECVAM (*The European Centre for the Validation of Alternative Methods)* must be allowed to comment on test proposals to ensure minimum animal usage.

To receive the ECEAE's full opinion please contact me on the e-mail or mail addresses given below.

New Commission Proposal on Plant Protection Products

On 17th July the Commission released their proposal for the overhaul of Plant Protection Product (pesticides) legislation to replace the 1991 directive. The legislation proposes a two-step procedure whereby individual active substances have to be approved and then plant protection products themselves have to be authorised.

The legislation contains some positive steps regarding data-sharing. For example, applications by companies for authorisation of their substance must include a report of the steps taken to avoid duplicate animal testing. However this could be strengthened.

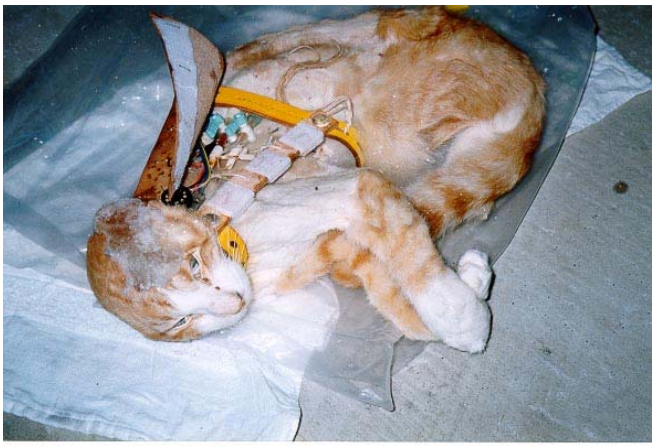
Furthermore, a recital stating that 'repetitions of studies involving vertebrates should be prohibited' that was included in an earlier draft from the Commission has been removed!

The proposal also fails to mention alternative non-animal testing methods. Alternatives are already in use with more becoming available regularly, reducing the use of many of animals. Every effort should be made to encourage the development and use of such methods, and legislation needs to support this.

For example the text states that submissions 'shall not contain any reports of tests or studies involving the deliberate administration of the active substance or the plant protection product to humans.'

However, microdosing is an alternative technique being developed at the moment which involves giving a few molecules of a substance to human volunteers. Completely harmless at this dose level, sensitive equipment can track how it interacts with the body.

Microdosing has been endorsed by the European Medicines Agency, the US Food and Drug Administration and there are increasing reports of its use within the pharmaceutical industry. The Commission proposal would outlaw the use of this technique. This must not happen.



Cats are routinely used in laboratories for safety testing on products designed for humans, despite significant differences between the species.

Close of 86/609 Directive Expert & Public Consultation

The nine-week public and stakeholder consultation by the Commission on the review of the 86/609 directive on the Protection of Animals Used in Experiments came to an end on August 18th. There were two questionnaires, one for members of the public and one for expert stakeholders. This is part of the impact assessment that started in January and is due to be completed in October 2006.

The Commission proposal is due out in the early part of next year.

Unnecessary Animal Testing - An Overview

A large proportion of animal tests are technically unnecessary, regardless of whether they work or not. These include tests that are:

1. Conducted at the same time as human tests
2. Not required by law
3. Never made public
4. Duplicated
5. Could be replaced (alternatives)
6. Have been replaced but not yet accepted

1. Conducted at the same time as human tests:

During drug development, the long-term animal toxicity studies are often still underway during human trials[1].

A number of reviews of human drugs have looked at how relevant the animal tests were in terms of providing information about safety and efficacy. Apart from major discrepancies in results between the animal studies and the human clinical trials[2], these also repeatedly found that the animal studies had continued for years after they were tested in humans[3-5].

2. Not required by law

It is often forgotten that the great majority of animal tests are not required by law. Only safety testing of chemicals, pesticides, biocides and medicines are 'required' by the regulatory bodies who determine the safety of new products. All other types of animal use (such as basic research and education) are not 'required' by an external body. Much of this is the breeding of GM animals who may then be used to 'screen' drugs for efficacy. Particularly within universities, research tends to be performed on more of an ad-hoc basis depending on the researchers' own interests, rather than under any great public health strategy. Nonetheless this constitutes a large proportion of animal use (43% in the UK in 2005)[7].

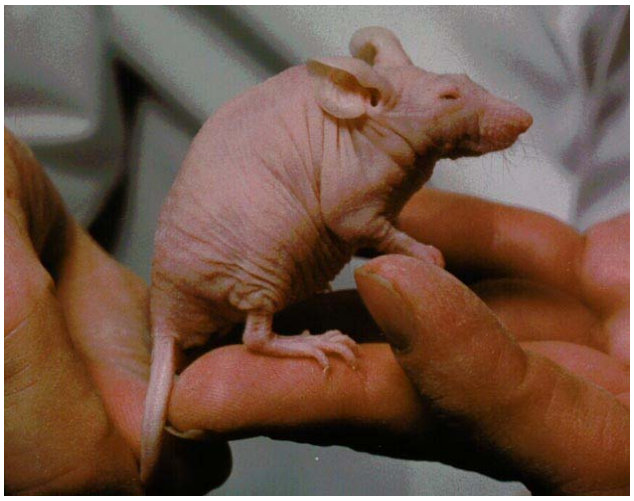
3. Never made public

It is also well known that a large proportion of animal tests are never published. Currently, animal tests that assess the efficacy and the safety of chemicals and drugs are rarely published for commercial reasons. Whilst these have arguably 'served their purpose' in this instance, for non-regulatory research failure to publish is a major concern. This means that the results of the tests are not available for wider dissemination by other researchers or health care professionals. Not only can this lead to duplication of animal tests (see below) but it means that whatever was learned is never passed on.

This partly arises because scientific journals are restricted in what they can publish and tend to prefer to publish novel techniques and successful trials. Failure to find the answer they were looking for, often referred to as 'negative results', or experiments that 'go wrong' or lead down 'blind alleys' are therefore frequently not published[8]. The same is true in drug development, except perhaps when a drug successfully passes the animal tests. Given that 'only 5 of the 5,000 compounds that enter preclinical (animal) testing go on to human trials'[9], this is likely to be a tiny proportion of the actual animal tests that go on. At the moment it is very difficult to work out how many studies never get published because the system is so secret. The ECEAE is pushing for the creation of a database of all animal experiments so that not only will tests not be duplicated but they will be allowed to undergo independent scrutiny.

A growing number of analyses are coming up with disturbing findings that suggest that even those studies that do get published are never used by others[12]. Citation analyses use databases to count how many other researchers have quoted the original piece of work. A highly useful piece of work will be quoted by many authors. These researchers found that even studies for medical interventions were rarely cited in human medical

journals, suggesting that they were not used to help inform human medicine.



Genetic engineering studies already use a huge number of animals and the number is predicted to sharply increase unless controls are put in place.

4. Duplicated animal tests

Because of the failure to publish the results of animal tests (regulatory and research based) there are concerns that tests are being duplicated[8,13,14]. In order to ensure that this does not happen under the proposed REACH chemicals legislation, mandatory data sharing is being proposed. Under the US High Production Volume Challenge Program for chemicals, companies were required to publish proposed test plans for a limited period. This enabled other companies and individuals to alert the testing company and regulator where the data had already been generated, reducing the number of animal tests that had to be performed[15].

Duplication in the medical and basic research fields can also occur when researchers are following a similar line of inquiry. Either within their own research or in comparison to other research groups there is often a great deal of duplication of studies where only minor changes have been made, for example, slightly different drugs used, different doses, or different species of animal. This also occurs when similar drugs are developed by competing drug companies. Whilst the extent of the degree of duplication can vary, what is often lacking is an overall sense of the importance of the new piece of research, especially in terms of the animal suffering.

5. Test that could be replaced with non-animal methods

There is a huge range of alternative methods available.

Toxicology and drug development are two areas which have particularly benefited from the search for non-animal alternatives. There is a growing drive to replace animal safety tests for chemicals, cosmetics and drugs. The pace has been forced by animal protection groups reflecting strong public concern about animal experiments.

Sadly, there is no parallel legislative drive to develop and use non-animal methods in basic medical research carried out in universities and government laboratories. Consequently, most replacement methods in this field are discovered in an *ad hoc* manner. Commonly, time and funding constraints limit the design of in-house alternatives for each research project[17].

Under EU legislation, animal researchers are obliged to use alternatives in preference to animals[18]. Researchers are expected to show in their application for a new animal test that they have looked for alternatives and that there are none. In practice this relies on the skills of the researcher in searching for alternatives and the assumption that all alternatives are well publicised.

In some cases there genuinely is no alternative in their narrow field of interest. But what appears to be generally lacking is an overall appreciation of:

a) Other ways of answering the same question (e.g. what causes Parkinson' disease) which may be radically different e.g. population studies, human imaging studies.
b) How valuable this piece of research is likely to be.

This partly relates to publication, see above. Currently there is no overall accepted method for

evaluating how valuable a piece of research is[20]. Particularly with basic research where the outcome may not be appreciated at all, for a long time or may not lead to any kind of human health benefit, evaluating the overall value of the research is very difficult[8]. For this reason it becomes irrefutably unethical to conduct invasive research on animals when the benefits cannot even be measured let alone realised. (This is regardless of whether you accept that the whole cost to the animal versus benefit to us is a morally acceptable method of justifying animal experiments).

6. Have been replaced but are not accepted

Within the drug and chemical safety field there are processes in place for the acceptance of non-animal, in-vitro or refined (i.e. kinder) tests in place of the original animal tests. It is often these that the government likes to talk about. However, in practice 'regulatory acceptance' of alternatives can be slow. This is very frustrating as we know that the original animal tests have never had to go through this process. In practice, when validated alternatives do become available, the government, EU and international regulators typically drag their feet in ensuring that these are implemented and the associated animal tests are no longer licensed. This happened with the alternative to the ascites method for creating monoclonal antibodies[21], and is currently happening with an alternative to mice for testing shellfish toxins[22], and the MAPREC safety test for polio vaccines[23].

Governments should tackle each of these points to ensure that unnecessary animal testing is kept to a minimum. The revision of Directive 86/609/EEC on the protection of animals used for experimental and other scientific purposes that is currently underway provides the ideal opportunity to address these issues.

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6. Check the website for our upcoming Recreational Drugs report for classic examples of this.
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21. See http://www.buav.org/press/2001/01-29.html
22. See http://www.buav.org/campaigns/shellfish/index.html
23. See Next of Kin Report; http://www.buav.org/primates/downloads/BUAVNextofKinreport.pdf