Risiken erkennen – Gesundheit schützen

5th World Congress on Alternatives and Animal Use in the Life Sciences

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The World Congresses on Alternatives and Animal Use in the Life Sciences have been staged every three years since 1993 (1993 Baltimore, 1996 Utrecht, 1999 Bolognia, 2002 New Orleans). The goal of the World Congresses is to promote research into alternatives to animal experiments around the world.

The World Congresses are intended for very different interest groups:

1. The international welfare movement which has introduced discussions on reducing or completely ending animal experiments into social dialogue for more than 30 years;

2. Scientists involved in animal experiments who use scientific and legal arguments to justify them;

3. Public agencies which prescribe the conducting of toxicological safety animal experiments on the grounds of consumer and environmental protection;

4. Industrial enterprises which do animal experiments when developing new products and which also have to conduct animal experiments in order to prove the efficacy and safety of new substances and products in line with international statutory provisions.

The 5th World Congress is staged in Berlin from 21-25 August 2005. ZEBET (Centre for Documentation and Evaluation of Alternatives to Animal Experiments) within the Federal Institute for Risk Assessment (BfR) is the co-organiser of the Congress. The 5th World Congress is organised by the American foundation ACT (Alternatives Congress Trust). The Foundation administers the funds donated by animal welfare organisations, industry and state institutions for the purposes of increasing the use of alternatives to animal experiments.

Criticism of animal experiments

Both within the EU and on the global level, criticism of animal experiments is mainly directed at the toxicological safety tests prescribed by public agencies like the ones stipulated in conjunction with the development of medicinal products, plant protection agents, industrial chemicals and cosmetics.

Around the world animal experiments to develop medicinal products to treat life-threatening diseases in man are generally accepted irrespective of the burden for the experimental animals. Up to now animal experiments have been essential for the development of medicinal products because it was not possible to prove they were safe for man without them. The infection tests that have to be conducted when developing vaccines are particularly distressing for animals because the efficacy of the vaccines can only be proven in disease models in animal experiments.

The situation is completely different when it comes to developing substances and products which "merely" serve to improve the life quality of man, for instance cosmetics. That's why the animal welfare movement around the world has focused its criticism on animal experiments for the development of cosmetics. The public at large shares this criticism although scarcely any animal experiments of this kind are conducted any more in Europe.

For more than two decades the European Commission has set itself the goal of reducing animal experiments in conjunction with the development of cosmetic products. The 7th Amendment to the EU Cosmetics Regulation (EU Directive 2003/15/EC) envisages an end to toxicological safety animal experiments for cosmetics and their ingredients within the next 12 years. This political goal now enjoys the support of consumers all over the world which means that the major global cosmetic companies and the international cosmetics associations feel themselves to be bound by this goal.

For the above reasons, the European Commission but also the German Federal Research Ministry have made research funds available over the last 20 years for the development of non-animal alternatives for toxicological safety tests.

In Europe work has been ongoing since 2001 on the new chemicals legislation REACH (Registration, Evaluation and Authorisation of Chemicals) concerning the handling of chemical substances. Amongst other things, the proposal for new European chemicals legislation envisages the toxicological assessment of around 100,000 chemical substances which are marketed in Europe. Even if a basic toxicological dataset were to be prepared for only the 30,000 most important industrial chemicals, animal experiments would have to be conducted on a large scale in order to close the existing information gaps. Against this backdrop the chemical industry, particularly for economic reasons, calls for as wide as possible a renunciation of animal experiments and the securing of the missing toxicological data by means of non-animal alternatives. The animal welfare movement makes the same demand on ethical grounds. The European Commission has taken on board the scientific challenge posed down by the new REACH legislation and is currently examining whether the elaboration of the basic toxicological data for industrial chemicals is possible with test methods involving no animal experiments. Of course, alternative toxicological methods have to be developed and experimentally validated to meet this scientific challenge.

Centres for the development of alternative methods

EU Directive 86/609 for the protection of experimental animals stipulates that no animal experiments may ever be conducted when an alternative, non-animal method is available. In order to put flesh on the skeleton of this legislation dating back to 1986, EU Member States have set up scientific centres for the development of alternatives to animal experiments with the emphasis on replacing the particularly distressing toxicological animal experiments in the eye/mucous membranes and the LD_{50} tests.

With the establishment of ZEBET (Centre for Documentation and Evaluation of Alternatives to Animal Experiments) in 1989 in the former Federal Health Office (BGA), Germany became the first country to set up a state centre for the development and validation of alternative methods. Today, ZEBET is based in the Federal Institute for Risk Assessment (BfR). In 1992 the EU set up the EU validation centre ECVAM (European Centre for the Validation of Alternative Methods) in Ispra (Italy). The USA opened its validation centre ICCVAM (Interagency Coordinating Committee on the Validation of Alternative Methods) in 1996. In response to the success of these centres other EU Member States have since developed comparable centres, for instance the Netherlands, the United Kingdom and France. In Japan a Centre for Alternative Methods was created on 1 December 2005 within the national health office.

The 3R Principle of Russel & Burch

In 1959 William Russel and Rex Burch in England outlined the 3R Principle (Replace, Reduce, Refine) for the development of alternatives in their book "The Principles of Humane Experimental Technique". The 3-R Principle proposes

- replacing animal experiments,
- reducing the number of animals,
- refining the pain and suffering of experimental animals by less aggressive, less distressing tests.

In the Anglo-America world the 3R Principle became established in the 1980s thanks to the active support of scientific centres like CAAT (Centre for Alternatives to Animal Testing) at the Johns Hopkins University in Baltimore (USA) and Frame (Fund for the Replacement of Animals in Medical Experiments) in Nottingham (UK). The World Congresses on Alternatives to Animal Experiments have contributed to this concept now being recognised as binding by the most important institutes involved in research in the natural sciences. For instance, in 2001 the European Science Foundation (ESF) took over the 3R Principle as its model for research. ESF is a merger of all research-promoting institutes in Europe. In Germany its members include the German Research Foundation (DFG) and the Max Planck Society (MPG). Independently of this, the NIH (National Institutes of Health) took over the 3R Principle into its support guidelines more than 10 years ago.

Success in securing acceptance by public agencies of non-animal toxicological test methods

The animal experiments laid down by public agencies have been harmonised (standardised) on the supranational level as EU Test Guidelines and on the international level by the Organisation for Economic Co-operation and Development (OECD Test Guidelines).

In order to replace the animal experiments stipulated by public agencies with non-animal alternatives, the new methods must first be validated in experiments. The first step involves examining in interlaboratory tests whether the methods lead to the same results in all laboratories around the world. A second step involves examining whether the results correctly predict a specific toxicological effect in man or in animals. There are now a large number of highly promising cell culture modules which supply reproducible results; however only a few of them are suitable for toxicity testing. With the non-animal methods it must be possible to classify and label chemical substances for the purposes of protection at work and consumer protection in the same way as was possible up to now with the results from animal experiments.

The staging of validation studies takes a great deal of time and money. Hence only few alternative methods have been successfully validated up to now and then accepted internationally. ZEBET, in co-operation with the EU validation centre ECVAM, has co-ordinated these activities and secured the financing of validation studies. The following four *in vitro* methods were accepted in 2002 after successful validation as EU test methods:
1. Corrosive effect on the skin (two methods)
2. Phototoxicity testing (one method)
3. Testing for skin absorption (one method)

These test methods were also accepted in 2004 by OECD for global use. The European validation centres, ECVAM and ZEBET, have thus proved for the first time scientifically that

alternative toxicological test methods are applicable for public agency purposes. This meant that the dogma of the essential need for animal experiments for individual areas could be refuted. Of course, further intensive research and financial support for validation studies will be required before more complex toxicological methods can be replaced by non-animal methods.

Topical themes at the 5th World Congress

Given the growing topicality of the development of alternative methods based on the 3R Principle, the 5th World Congress on Alternatives and Animal Use in the Life Sciences is supported by important state research institutes like NIH from the USA, the Home Office in the United Kingdom and the German Federal Ministries of Consumer Protection, Food and Agriculture (BMVEL) and Education and Research (BMBF).

These bodies not only support the participation of international renowned scientists but also provide grants above all for the participation of young scientists from the new EU Member States as well as from Asia and South America. The goal is to promote international acceptance of the 3R Principle.

Against the backdrop of the 7th Amendment to the EU Cosmetics Directive, the cosmetics industry uses the 5th World Congress in Berlin as a forum in order to present to the scientific public at large the progress made in the development of toxicological safety test methods for cosmetics and their ingredients. The European Cosmetic, Toiletry and Perfumery Association "colipa" plays a major part in the 5th World Congress. The major manufacturers of cosmetics and their ingredients (L'Oreal, Procter & Gamble, Unilever, SHISEIDO, Henkel, Beiersdorf) are also the main sponsors of the Berlin Congress. Several of these firms will present their own research projects for the development of alternative test methods at the 5th World Congress.

It is not, therefore, surprising that more than 10% of the 600 papers and poster presentations at the 5th World Congress address *in vitro* methods for skin tolerance testing.

Given the extensive discussions of alternative methods within the framework of the EU chemicals legislation REACH, the chemical industry contributes both to the funding and the content of this year's Congress as does the medicinal product industry.

In the same way as the previous World Congresses on Alternatives and Animal Use in the Life Sciences, the 5th World Congress also enjoys special financial support from the international animal welfare movement. Hence, the main emphasis of the Congress is on the establishment of the 3R Principle in university disciplines (biology, medicine, veterinary medicine), ethical discussions of animal welfare in the field of experimental animals, ethical-moral concepts for handling animals as fellow creatures and the further development of information offerings on alternative methods.

One new focus of the 5th World Congress is on computer-aided methods for the prediction of toxic effects (QSAR – structure-activity relationships) as well as the use of information on the Internet by scientists who wish to work with methods which reduce the suffering of experimental animals in accordance with the 3R Principle.

Organisation of the 5th World Congress

The 5th World Congress – like the 4th World Congress - is organised by the American foundation ACT (Alternatives Congress Trust) which is based in Washington DC. The Foundation administers the funds donated by the animal welfare movement, industry and state agencies. The financial set up of the Foundation is such that it is in a position to reduce the risk for the respective organisers. ACT has the goal of disseminating the scientific concept of the 3R Principle around the world. To this end, the World Congresses are the ideal medium. Besides the exchange of ideas between established scientists, young scientists are to be introduced to this new scientific field.

It is particularly satisfying that our Japanese colleagues from JSAAE (Japanese Society for Alternatives to Animal Experiments) have already indicated that they will stage the next World Congress in Tokyo. ACT hopes that, in this way, the ethical principles developed in Europe for the protection of experimental animals will be quickly introduced into the emerging countries in the Asia-Pacific region.

Presentation of the 24th Animal Welfare Research Prize of the Federal Government to Dr. Christoph Helma

The Federal Minister of Consumer Protection, Renate Künast, will present the Animal Welfare Research Prize of the Federal Government 2004 during the opening ceremony of the 5th World Congress to Dr. Christoph Helma (Freiburg University) which comes with € 15,000.

Helma receives this award for the development of an inductive database for the prediction of carcinogenic substances. The new system for the analysis of structure-activity relationships (SARs) aims to contribute to reducing animal experiments for public agency purposes as planned within the framework of the new EU chemicals legislation REACH and the 7th Amendment to the EU Cosmetics Directive.

The lazar programme (lazy structure-activity relationships) developed by Helma extracts the chemical compounds already tested in animal experiments from a database which are most similar to the structure of a new compound and uses this information to predict toxic properties. The new feature of lazar is that the similarity between two chemical substances is always restricted to one toxic property. For instance, two substances which have very similar properties when determining toxicity may, at the same time, have different carcinogenic properties.

With the help of this new method existing experimental data, accessible in large, international databases can be used in a more targeted and more problem-related manner than in the past to predict the harmful properties of chemicals. In this way the system makes an important contribution to making better use of existing knowledge which helps to further reduce the number of animal experiments needed.