ZEBET's Role as National Focal Point for Stakeholders:
View of ZEBET Commission Members

Heidemarie Ratsch; representative for the states of the Federal Republic of Germany and the competent authorities concerning the authorisation of experiments on animals

First of all I would like to congratulate ZEBET on its 20th anniversary on behalf of my colleagues from the competent authorities. Despite the many difficulties caused by political turbulence as well as a variety financial problems, ZEBET seems today much stronger and more effective than ever before. I therefore want to express my sincere hope that the worst is over. This hope is based on the recent successful activities of ZEBET especially within this past year. These activities include the workshops concerning transgenic animals and botulinum toxin in addition to other seminars concerned with in vitro methods. I would also like to mention the support of ZEBET employees regarding the proposal of the Directive on the protection of animals used for scientific purposes.

- **How are the competent authorities affected by the efficiency of ZEBET?**

To answer this question I'd first like to point out the importance of ZEBET for the authorities who are required to licence experiments on animals.

Since 1986 the German Animal Welfare Act has ensured that experiments on animals shall only be allowed if no other methods or procedures are available to achieve the same purpose. A thorough and competent review must be completed by both the applicant and the competent authority. This legal mandate involves not only experiments on animals which require a licence but also experiments not requiring a licence but which nevertheless must be declared. Especially after the inclusion of animal welfare in the German Constitution in 2002, the competent authorities are now more responsible to question the statements, the research and the data of all applicants.

To understand the enormity of this responsibility you have to know, that every year, in Berlin alone, nearly 400 projects are submitted.

To accommodate these 400 submissions, there are only three available veterinarians. And this particular task comprises only one of their assortment of responsibilities.
Despite our best efforts the number of animals used in scientific procedures rises every year.

In Germany the competent authority is fortunate to have a commission which gives its support in deciding whether to authorize experiments on animals. But nearly one third of all registered projects don't need an authorization and therefore aren't seen by the commission. Nevertheless, we have to verify that all experiments have no other alternative besides using animals.

Apart from the replacement of animals in experiments one must also take into account two other factors. First, reducing the number of animals used in procedures and second refining the methods of experiments in order to minimize pain and suffering, especially in view of the revision of EU Directive 86/609.

In the competent authorities the decisions are usually made by veterinarians. But the education and training of these veterinarians especially concerning laboratory animal science is at different levels. And their tasks, which have to be fulfilled, are just one part of the veterinarian's responsibilities. Consequently, there isn't a lot of time to make extensive investigations into alternative methods of experimentation.

ZEBET was established to provide help in all these affairs, particularly in the form of written statements declaring whether or not there are alternative methods of experimentation. In our discussions with applicants, ZEBET's statements carry considerable credibility.

From ZEBET's 2005 report I know that only 2% of the inquiries came from the authorities of the federal states; 9 cases from a total of 454 cases.
We have 16 federal states in Germany and about 30 authorities are responsible for the licensing of experiments on animals. What would happen if each competent authority asks for help only in one or even more than one case per year?

- **For that reason our main question becomes: Can ZEBET ensure the answer in time?** Why is time a relevant factor?

Approvals must be granted within a period of three months. Actually, the period is prolonged if there are questions to the applicant, but the inclusion of ZEBET by the authority, doesn't count in terms of the deadline.

Even more alarming, experiments for which only a notification is required must be handled within a period of only two weeks. The only possibility of stopping the time limit is to prohibit the experiments if any question remains open.

The competent authorities have had different experiences concerning the time ZEBET requires for the assessment of a request.

Especially in recent years the shortage of ZEBET employees has resulted in the delay of their response, so that some colleagues from the competent authorities lost the hope to get the answers early enough and consequently didn't ask ZEBET anymore.

On the other hand it is also said that very helpful information was given by phone and per e-mail in a rather uncomplicated way without a lot of red tape.

But what we need is a reliable and predictable partnership. Reliable in the sense that the statements will come and predictable in the sense that they will come on time. To ensure this, it should be established in the mission statement of ZEBET how to deal with these issues.

Another problem is the limited alternatives which ZEBET is able to recommend in the area of basic or applied clinical research. Commonly, there are no alternatives available. But especially in procedures inflicting severe pain, suffering and harm to the animal, we always try to discover methods which will eliminate or reduce any possible pain, suffering and harm to a minimum. In this regard, ZEBET could be a great support in realizing the effective refinement of research methods.

The number of animals used in projects has to be reduced to the absolute minimum without compromising the objectives of the project. Sometimes it is possible to get the same or even better results by changing the normal procedure.
Who if not ZEBET with its worldwide network is better equipped to find a way to use the least number of animals in experiments and, additionally, how to inflict the least amount of pain on the animals that are used in experiments.

I want to point out some examples which have been given to me from my colleagues. ZEBET was extremely helpful by refusing the twofold reproduction of experiments within a project dealing with a tumour model. On the basis of a brilliantly researched statement, the competent authority could successfully argue in favour of reducing the amount of mice from 2688 to 1412. Additionally, a valuable recommendation in terms of refinement was given concerning the overall construction of the experiment which could be implemented. This statement was requested within a very short time limit and it arrived on schedule. My colleagues were very pleased.

Other demands for help referred to

- the necessity of death as endpoint concerning the development of vaccines
- repeated retro bulbar taking of blood samples
- hypothermia as anaesthesia for newborn mice and
- the production of monoclonal antibodies using the ascites method

In all these cases the demanding authority received excellent advice.

But we also had the unfortunate experience in which no help was possible in connection with basic research such as activity measures from single brain cells using monkeys or rats. And there are still no alternatives for experiments concerning cardiac infarction or stroke; diabetes or high blood pressure. A lot more examples could be given.

But as I mentioned a few moments ago we are not only being asked to replace experiments on animals but also to reduce the number of test animals to the absolute minimum. Additionally, we are being asked to ensure that all possible pain and

suffering of the animal is reduced to a minimum. Lastly, we are being asked to improve the care, treatment and living conditions of the animals to enhance their well-being.

As a client of ZEBET the competent authorities would like to receive the following products:

- advice and support especially in the form of written statements for alternative test methods to experiments requiring a licence, as well as to experiments which need only to be notified
- statements with reference to the refinement of experiments, for example using a smaller number of animals or less stressful methods
- aid regarding the differentiation between legally prescribed experiments and experiments requiring a licence, in particular by finding the relevant regulations like OECD- or ICH-Guidelines or European legal norms
- concerning the use of the ZEBET database, it would be extremely helpful if the database could be widened about 3R-methods in basic research
- expansion of the tasks of ZEBET on the subject of refinement related to the living conditions of laboratory animals
- assignment of specific contact persons to strengthen the cooperation between ZEBET and the competent authorities
- additional support through research of 3R-methods in areas where particularly high numbers of animals will be used or very harmful experiments will be conducted

I'm glad to see that ZEBET is beginning to consider methods of reduction and refinement of the conditions under which the animals are currently being tested. It is also encouraging to see that these issues are receiving greater attention than they ever have. We can find these objectives expressed on the ZEBET homepage. Moreover the personnel situation has been eased by appointment of Sarah Adler and Michael Oelgeschläger as contact persons for official statements regarding authorization procedures of animal experiments.

So allow me to conclude with a quotation from the proposal for a new directive on the protection of animals used for scientific purposes:

The ultimate goal should be to replace the use of animal experiments all together. In addition to animal welfare benefits, alternative methods also have the potential to provide robust information through quality-controlled, state-of-the-art tests which could be faster and less cost-intensive than classical animal-based tests.

Best wishes again for the future of ZEBET!