



Information Retrieval on Alternative Methods to Animal Experiments – One of the Factors that Affect Implementation of the Three Rs in Research and Testing

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Summary

Both high quality research and the protection of animals used for scientific purposes demand application of the best tools to ensure that the 3Rs are appropriately considered and realized. The decision as to whether or not an animal experiment is indispensable is based on the state of the scientific knowledge and a scientific determination of whether the pursued purpose cannot be achieved by alternative methods. In this context, searching high-value information on alternatives to animal testing is one of the key elements to establish the indispensability of an animal experiment. To improve dissemination of alternative methods at the national level, the German Centre for the Documentation and Evaluation of Alternative Methods to Animal Experiments (ZEBET) pursues a three-fold strategy that consists of 1) capture and supply of information via the AnimAlt-ZEBET database, 2) education in systematic search procedures, and 3) research in retrieval technology.

Keywords: animal protection legislation, 3Rs concept, information retrieval, indispensability search

1 Introduction

High quality information on alternative methods is crucial for scientific reasoning regarding the necessity of performing an experiment using animals. Here, scientific evidence serves to verify the project's compliance with the requirements of the 3Rs, which is a prerequisite for authorization of animal experiments according to the European legislation covering the use of animals for scientific purposes. This obligation complies with the internationally accepted 3Rs concept (*Replace, Reduce, and Refine*) that was laid down by Bill Russell and Rex Burch (1959).

In 2010 the EU adopted the revised Directive 2010/63/EU on the protection of animals used for scientific purposes, which replaces Directive 86/609/EEC. The new Directive prescribes procedures regarding the authorization and evaluation of animal experiments, including information requirements to assess a project's compliance with the provisions of the 3Rs, which the EU Member States have to implement into national law.

According to the German Animal Protection Law (*Tierschutzgesetz*, 2006, amended 2009), for example, any person planning to conduct animal experiments must obtain authorization from the competent authority. Application for authorization of a planned animal experiment includes scientific evidence that the experiment is indispensable. The applying scientist must consider the state of the relevant scientific knowledge and examine whether the pursued purpose cannot be achieved by alternative methods. Based on the written application form,

competent authorities check the application and decide on the project.

According to a legal commentary on the German Animal Protection Law, an application for project authorization is defined as a conclusive "statement of facts" that has to meet professional standards (Lorz and Metzger, 2008). In the area of jurisprudence a statement of facts is a legal document that gives a generally valid description of a particular situation and relates this to the pertaining regulation (Smidt, 1983). In contrast, in the life sciences, scientists do not supply uniform and generally agreed-upon forms of verification of the necessity of performing experiments using animals. Scientific evidence of the indispensability of animal experiments is given on an individual basis. Thus, legislative authority links general legal standards for the protection of animals with scientific evidence of the necessity of an individual animal experiment.

The examination of whether or not the pursued scientific goal cannot be achieved by alternative methods is a key element in the application of a planned animal experiment. It includes, as a first step, the search for high-value information on alternatives to animal testing.

To improve dissemination of alternative methods, the Centre for the Documentation and Evaluation of Alternative Methods to Animal Experiments (ZEBET) at the Federal Institute for Risk Assessment in Berlin, Germany, is committed to a strategy that consists of the following three components: 1) supply value-added information, 2) educate in systematic search procedures, and 3) research retrieval technology (Butzke et al., 2010).



2 Supply with value-added information

ZEBET provides free online access to its value-added database, *AnimAlt-ZEBET*. It is a full-text database of evaluated alternative methods to animal experiments. All documents are written in a structured and standardized manner and concentrate on the most essential facts of a given alternative method. The added value of *AnimAlt-ZEBET* documents is constituted through expert selection of incorporated literature dedicated to the most substantial and reliable information. Furthermore, the summaries aim to enable users to consider the suitability of the method at hand for their own purposes without the need to collect additional information. Therefore, *AnimAlt-ZEBET* serves as convenient starting point, especially for scientists and authorizing bodies, to perform a structured search for information on suitable alternatives to a particular animal experiment.

When an individual document is accessed, the user will find the key information at a glance. To obtain a general idea of the method at hand, the reader can consult the meta-data fields: "Title," "Evaluation," "Status," and "Regulation," in combination with the abstract section "3R relevance." Here users will find highlighted facts that describe the specific objective addressed by the method, its state of development, acceptance in the scientific/regulatory community, application domain, and contribution to the 3Rs concept.

Composition and phrasing of the method summaries are standardized to enable immediate orientation and easy comprehension and to provide possible feedstock for up-to-date text mining applications. The main text of the method summary aims to cover all aspects necessary for drawing a conclusion regarding the suitability/applicability of a particular method in a given context. Thus, the focus is on practical considerations, e.g., endpoints, operating schedule, required equipment, limitations, etc. The section "Expert Panel Opinions" provides a detailed picture of the acceptance of a particular approach and possible objections that might be raised by official bodies. In the basic sciences, where there are no official bodies in place to evaluate the merit of scientific methods, the impact of a method is judged by bibliometric analyses, i.e. citation analyses, impact factor of the publishing journal, etc.

The workflow of method-portray production integrates a peer review process performed by highly regarded experts in the field. The decision as to which method should be portrayed in *AnimAlt-ZEBET* next is triggered by the urgency of the topic/issue to be addressed (e.g., increase in the number of animal experiments in the field of neurodegenerative disease research) and whether there are ongoing requests for a review on animal use application by national authorizing bodies.

*AnimAlt-ZEBET*¹ is hosted by the German Institute of Medical Documentation and Information (DIMDI). At this resource users can search the database exclusively or – in a "superbase mode" – combined with other databases like PubMed.

¹ <http://www.dimdi.de/static/en/db/dbinfo/zt00.htm>

² <http://www.gv-solas.de/aus/aus/index.html>

³ http://www.dfg.de/download/pdf/foerderung/rechtliche_rahmenbedingungen/gute_wissenschaftliche_praxis/self_regulation_98.pdf

3 Education in systematic search procedures

High quality information on alternative methods is critical for scientific reasoning on the necessity of performing experiments using animals. In co-operation with universities and the Regional Authority for Health and Social Matters of Berlin (LAGeSo), ZEBET staff participates in training courses on "Laboratory Animals, Animal Experiments and Alternatives" that cover the topic of information retrieval procedures. This course is certified by the German Society for Laboratory Animal Science (GV-SOLAS)² according to the recommendations of the Federation of European Laboratory Animal Science Associations (FELASA) for education and training. The course is attended each year by some 200 to 300 scientists who are involved in animal experimentation.

Corresponding to the rules of good scientific practice of the German Research Council of 1998³, scientific information retrieval should adhere to professional standards. An internationally accepted standard for systematic search procedures has been set up by the Cochrane Collaboration (Higgins and Green, 2011). Highly sensitive search strategies retrieve the best evidence in Cochrane reviews of research in human health care. The current best evidence is up-to-date information from relevant, valid research.

The "Cochrane Information Retrieval Methods" serve as a role model for ZEBET's training courses. The contents of the information lesson, for example, include systematic searching, choosing the most relevant information resources, conceiving of search terms, using operators and wildcards, index-term-based searching, and semantic search engines. The basic consideration of any systematic search approach for alternative methods is an *a priori* identification of those features of a method that provide answers to the scientific questions of a research project. Since a number of reliable scientific resources provided free of charge, e.g., PubMed and Agricola, include index terms that – at least rudimentarily – cover the area of alternative methods, a major goal of the lesson is to instruct participants in index term-based searching strategies (Motschall and Falck-Ytter, 2005) and 3R-relevant terms.

4 Research in retrieval technology

The Internet enables access to an unlimited quantity of information on alternative methods to animal experimentation. However, it is still difficult to select the right pieces of information from this vast amount. Conventional search engines perform searches in free text or with given terms from a thesaurus. This is where semantic web technologies can foster serendipity and lead to much more targeted information. Semantic web technologies aim to gather the meaning of natural language documents or phrases from the occurrence and co-occurrence of certain terms and their synonyms within the text of documents.



One example of such an engine is the knowledge-based Go3R tool that aids in retrieving 3R-relevant literature from PubMed (Sauer et al., 2009). It is the first tool of its kind worldwide and is specially equipped with expert domain knowledge from the area of the 3Rs. This knowledge is captured within an “ontology,” i.e. an extensive and detailed network of “concepts” – terms that are unambiguous identifiers of the respective scientific domain, such as “gene chip” in the field of genetic high-throughput screening, or “humane endpoints” in the field of the 3Rs. When a user performs a search query with Go3R, the search engine compares the concepts of the ontology with the vocabulary used in the retrieved documents (Sauer et al., 2009). It highlights relevant terms or their synonyms and uses them to arrange the documents within an “intelligent” directory of contents. The directory is presented alongside the search results and serves as a convenient means of navigation.

The Go3R search engine has been developed by scientists from the Technical University Dresden and the Transinsight GmbH (Dresden) in cooperation with ZEBET, BASF – The Chemical Company, and the Scientific Consultancy – Animal Welfare (Neubiberg). The beta-version is available online free of charge⁴.

This beta-Version currently contains more than 17,000 concepts structured into 23 branches with biomedical headings, e.g., “Cell Culture Technology,” “3Rs Methods in the Life Sciences,” etc. Thanks to funding from the German Federal Ministry of Education and Research (BMBF), the search engine will be re-engineered and extended to meet the requirements of scientists and competent authorities even better. As of July 2011, Go3R also searches both in PubMed and in the TOXLINE® database as additional scientific resources.

Based on the experiences of the Go3R project, ZEBET is currently setting up the next research project. Laboratory animal scientists, animal welfare officers, competent authorities, information scientists, and ontologists are engaged in the joint research project “Development of an Ontology on the Severity Classification of Scientific Procedures with Animals” according to Directive 2010/63/EU, Annex VIII “Severity Classification of Procedures.” The purpose of the project is to verify the concept of ontological modeling of assignment criteria for severity classification.

5 Conclusion

Scientific discourse on the indispensability of animal experiments requires access to and proper use of results from high quality research. This access also lays the groundwork for up-to-date, well-informed and objective-driven science.

Against this background it becomes clear that the improvement of information retrieval of alternative methods requires a multitude of efforts. These include the implementation of high-grade education in this field, intensive research in retrieval tech-

niques, and access to value-added information.

With its three-fold strategy covering information, education, and research ZEBET strives to assist scientists to conduct well-informed research and has done so for some 20 years.

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⁴ www.Go3R.org