

Current Status and Future Developments of Databases on Alternative Methods

The Report and Recommendations of ECVAM Workshop 25^{1,2}

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Preface

This is the report of the twenty-fifth of a series of workshops organised by the European Centre for the Validation of Alternative Methods (ECVAM). ECVAM's main goal, as defined in 1993 by its Scientific Advisory Committee, is to promote the scientific and regulatory acceptance of alternative methods which are of importance to the biosciences and which reduce, refine or replace the use of laboratory animals. One of the first priorities set by ECVAM was the implementation of procedures which would enable it to become well-informed about the state-of-the-art of non-animal test development and validation, and the potential for the possible incorporation of alternative tests into regulatory procedures. It was decided that this would be best achieved by the organisation of ECVAM workshops on specific topics, at which small

groups of invited experts would review the current status of various types of *in vitro* tests and their potential uses, and make recommendations about the best ways forward (1).

The workshop on the Current Status and Future Developments of Databases on Alternative Methods was held in Neubiberg, Germany, on 12–15 September 1996, under the co-chairmanship of Margot van der Kamp (Netherlands Centre Alternatives to Animal Use, Utrecht, The Netherlands) and Annett Janusch (ECVAM, Ispra, Italy). It was organised by Ms van der Kamp and Roman Kolar (Akademie für Tierschutz, Neubiberg, Germany). This ECVAM workshop was the first official meeting of experts who have been involved in the creation and maintenance of databases which contribute to the Three Rs (reduction, refinement, replacement) of Russell & Burch (2). The key objec-

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¹ECVAM — European Centre for the Validation of Alternative Methods. ²This document represents the agreed report of the participants as individual scientists.

tives of the workshop were to bring together these experts to: a) review the current situation; b) identify the types of information needed which are not yet available from existing information services; c) discuss possibilities for cooperation and collaboration; and d) agree upon strategies for improving the dissemination of information on alternatives.

Introduction

It is a fundamental requirement that any scientist who intends to start a new project is well-informed about the current status of the proposed field of investigation. Animals should only be used in a study if such use is justifiable after all possible alternatives have been identified and found to be inadequate. Ready access to relevant information on the proposed topic of study can prevent the unnecessary duplication of work, thereby contributing to a reduction in animal use (3).

A major problem in any attempt to locate relevant information is the exponential increase in the number of scientific publications which has accompanied the development of science over the last four centuries (4). It has been estimated by Hans Kuiper (PREX, Utrecht University, The Netherlands) that at least 30,000 biomedical journals are currently being marketed, and that more than 3,000,000 articles are published annually in the biosciences. Technological advances which have increased the processing power and storage capacity of personal computers, together with improvements in the software used for searching electronic databases, offer a potential solution to this problem. However, these electronic resources are showing a similar proliferation, and thus it is becoming increasingly difficult to search for specific information (5). The identification of information relevant to the Three Rs is even more problematic due to further difficulties which are outlined below.

In recent years, electronic forms of both *bibliographic* databases, which contain references to publications, and *factual* databases, which contain original data and/or information on publications, have increasingly been developed in the various fields of bioscience (for example, *Agricultural Online Access* [AGRICOLA], BIOSIS, Current Contents, MEDLINE, European Chemicals Data and

Information Network [ECDIN] and the Registry of Toxic Effects of Chemical Substances [RTECS]). These databases can reduce the effort required to search for information on alternative methods, and they provide a wealth of data from many different fields of study (3).

The creation of "database hosts" by commercial or government concerns has provided one-point access to a variety of these databases. These hosts (for example, Deutsches Institut für Medizinische Dokumentation und Information [DIMDI], Dialog, DataStar, Scientific and Technical Information Network [STN] International and PREX) use predefined criteria to group databases in various subject areas. Some hosts permit the same search to be performed simultaneously in a large number of databases, for example, by using the "Superbase" mode in DIMDI.

Other very useful resources are also available, such as the quarterly annotated "Bibliotips" published by PREX, and the quarterly annotated bibliography *Alternatives to the Use of Live Vertebrates in Biomedical Research and Testing* produced by the US National Library of Medicine (NLM) from Medline and associated databases, which is available either through the Internet or as hard copy, on request.

Bibliographic and factual databases can be a powerful information tool, and database searches are an essential part of a stepwise approach to toxicity testing (6). The field of toxicology is, in fact, an area of continuous investigation (for example, by experts from the Toxicology Information Program of the NLM) with respect to the identification of new directions in database development for the storage and dissemination of toxicological information (7, 8). The use of public and in-house databases is a prerequisite to the research activities of every pharmaceutical company (9).

Keywords and indexing systems

Many bibliographic databases provide an abstract for each record, although this applies mainly to more-recent publications, since the practice until about 1985 was to assign keywords only, due to limitations of storage capacity. This may either be the abstract produced by the authors of the referenced document, or one written by abstractors working for the database pro-

ducer. The purpose of an abstract is to indicate the potential value of the document to a variety of users, but at the same time it may have to conform to stringent limitations with respect to length. To increase the information provided by the abstract, and to facilitate data retrieval, indexers add a number of relevant keywords and other index terms. These terms are frequently derived from indexing and classification systems defined by individual database producers, and are assigned to a document according to specific criteria (3).

Although the use of keywords is aimed at increasing searching power, the degree of success may be influenced by the level to which the searcher is familiar with the indexing system of the database concerned. Furthermore, the overlap in documents retrieved when the same search is performed on different databases may be low, as has been shown in comparative searches on MEDLINE, EMBASE and BIOSIS for methods to test for adverse effects on the skin and eye (10). The complexity of the enormous indexing systems required by databases covering the whole area of the biosciences may also give rise to inconsistencies in indexing quality. The net result is that some potentially relevant documents may not be retrieved and the performance of an exhaustive search may require an expertise that is not possessed by the average user (11).

The communication of information about non-animal alternatives is essential for the further development and validation of alternative methods (12). However, the search for literature pertinent to the Three Rs is associated with problems additional to those outlined above. It is very rare for any indication to be given that the content of a document could relate to an alternative method. The NLM has, as a first step, incorporated the terms "animal testing alternatives" and "animal welfare" into its Medical Subject Headings (MeSH) indexing system, and the AGRICOLA database has also adopted them. However, it is difficult to set criteria for assigning these terms, and they tend to be used more for the indexing of general discussions about the reduction and replacement of laboratory animal use than for the indexing of methodological papers. Indeed, the assignment of these terms to a methodological paper presupposes a deeper knowledge of a narrow field of study than might be expected

to be possessed by an indexer covering a large area within the biosciences. Thus, the existence of these terms may not have a very great impact on the success rate for the retrieval of specific information relating to the Three Rs.

These difficulties, together with the problem of the increasing quantity of scientific information and the growing demand from various quarters for access to recent developments in the area of alternatives, including information on validated methods or methods under validation, have led to the development of a number of specific databases by various national and international institutions (for example, 13, 14).

Information Services

The following brief survey of information services represented at the workshop reflects the current situation (mainly in Europe) of a number of databases and/or information services which have, in general, been created on an *ad hoc* basis to contribute to improving the dissemination of information on alternatives to animal experimentation.

Akademie für Tierschutz, Germany

The Akademie established a bibliographic database on alternatives, as defined by the Three Rs, in 1986. Print-outs of the database, dealing with specific topics, are published in hard copy as the "Gelbe Liste". The database contains about 15,000 references obtained from journals, conference reports and unpublished material, such as university course programmes. The database covers alternatives in education, including references to films, videos and computer simulations. The Akademie is funded by the Deutscher Tierschutzbund and the database was established originally to support the activities of this organisation (15–17). The database is available both on disk and online through PREX/NCA, but the Akademie also deals with direct queries (e-mail. akademie.fuer.tierschutz@muenchen.org).

Animal Welfare Information Center, USA

The Animal Welfare Information Center (AWIC) is part of the National Agricultural Library (NAL). The NAL produces the AGRICOLA database, which serves

researchers and others interested in the agricultural sciences and related subjects. The database is available through Dialog and PREX, and can also be obtained on CD-ROM. The establishment of AWIC was mandated in the 1985 amendment to the Animal Welfare Act. AWIC deals with about 1500 enquiries per year from veterinarians, scientists, animal technicians and curators, research administrators, federal regulators, congressional staff, students and the general public (18–20). It produces the *Animal Welfare Information Center Newsletter*, a number of information resources on animal welfare, and a CD-ROM with the full text of federal regulations, guidelines, policies, subject-related bibliographies, etc. AWIC publications are also accessible through AWIC's World Wide Web (the Web) home page (<http://www.nal.usda.gov/awic/awic.htm>).

ECVAM, Italy

ECVAM's Scientific Information Service is being established as one of the requirements of ECVAM within the European Commission, that is, to set up a database on alternative methods and their status. At present, the main activity is to develop a database to support validation studies carried out under the auspices of ECVAM. This database will provide information on all ongoing validation studies, with reference to the different stages of the validation process. It will include test protocols, information on the test chemicals, *in vivo* and *in vitro* data, the outcome of the data analysis, background documentation, and details of any potential follow-up activities. Initially, only selected information on current studies will be made generally available; however, full access will be permitted to information on completed studies. A hotline datalink for exchange of data via an intranet between participating laboratories is also envisaged (e-mail. annett.janusch@jrc.it).

Federal Veterinary Office, Switzerland

The documentation service of the Department of Animal Experimentation and Alternative Methods maintains a database of all animal experiments performed in Switzerland since 1992. Scientists are under a legal obligation to provide this information, which is used to produce statistical reports on laboratory animal use in Switzerland. There is

no public access to this database since much of the information is confidential. However, information is provided to external enquirers from a literature database of more than 4000 records on animal husbandry, alternatives, and the ethics of animal experimentation (e-mail. michelle.howald@bvet.admin.ch).

Galileo data bank, Italy

The Galileo data bank incorporates toxicology data (mainly on cosmetics) derived from studies with alternative methods (21–23). The data bank includes factual data on 821 ingredients, 322 cosmetic formulations, 54 test methods, 26 animal models, and 103 biological systems, with a total of nearly 21,000 individual results. The information is not currently available online, but print-outs are sent to enquirers. Although originally funded by DGXI of the European Commission and then by ECVAM, Galileo has not received funding since 1995, and its development is currently in abeyance.

INVITTOX, UK

This service, which was established by the Fund for the Replacement of Animals in Medical Experiments (FRAME) following a survey of potential users in 1986, provides protocols for methods of *in vitro* toxicity testing at a level of detail not normally found in the published literature. The 114 protocols available include those from recent validation studies coordinated by ECVAM. A total of 650 scientists, mainly from academia and industry, are registered to use the services of INVITTOX. Since 1990, about 5000 protocols have been sent out at the request of these users (11, 24). INVITTOX has been funded by DGXI and by ECVAM. It is being transferred from FRAME to ECVAM, and it is envisaged that the protocols will eventually be made available through the Internet (e-mail. invittox@frame-uk.demon.co.uk).

Multicenter Evaluation of In Vitro Cytotoxicity, Sweden

Between 1989 and 1996, 50 reference chemicals were tested for cytotoxicity in 96 different *in vitro* systems by about 50 laboratories worldwide, as part of the Multicenter Evaluation of *In Vitro* Cytotoxicity (MEIC) programme. CTLU (Cytotoxicology Laboratory, Uppsala, Sweden) is now in the process of publishing these results in ATLA (25–27). A

comparison of the results with acute human toxicity data is included, to evaluate the relevance of the *in vitro* tests. CTLU has also collected data on time-related toxic and lethal blood concentrations from acute human poisonings with the reference chemicals (the MEMO programme), to obtain reference values for the *in vitro/in vivo* comparisons. CTLU plans to disseminate the data from MEIC as well as from MEMO via the Internet. CTLU will also act as a clearing house, continuously extending and revising these databases (e-mail. bjoern.ekwall@ctlu.se).

Netherlands Centre Alternatives to Animal Use, The Netherlands

The Netherlands Centre Alternatives to Animal Use (NCA) is involved in several activities concerning databases on alternative methods, including managing a database of projects on the development and validation of alternative methods which are supported by its founder, the Dutch Alternatives to Animal Experiments Platform. NCA and PREX cooperate closely in disseminating information on alternatives (28, 29). Furthermore, the NCA has purchased rights to the database of the Akademie für Tierschutz and offers this information through the online service of PREX. The NCA Web site is at: <http://www.pdk.dgk.ruu.nl/nca>.

Norwegian Inventory of Audiovisuals

The Norwegian Inventory of Audiovisuals (NORINA) is an inventory of over 3500 audiovisual aids which could possibly replace the use of animals in teaching at all levels. It is available as an online version through the Web, through PREX, and as a disk version for purchase (30). It is one of the activities of the Laboratory Animal Unit at the Norwegian College of Veterinary Medicine, which is the national reference centre for laboratory animal science in Norway. The Web site is at: <http://oslovet.veths.no/NORINA>.

PREX, The Netherlands

PREX (part of the Department of Laboratory Animal Science, Utrecht University, The Netherlands) is an online information service that provides access via the Internet (using Telnet) to about 15 biomedical databases, including four major ones (MEDLINE, AGRICOLA, Cambridge Scientific Abstracts, and the CABI databases) and other smaller

databases concerned with laboratory animal science (books and conference proceedings). PREX merely provides access and the users must do their own searches. The online service is available by subscription; currently, PREX has about 200 subscribers in addition to local users at Utrecht University (e-mail. prex@pdk.dgk.ruu.nl).

University of California Center for Animal Alternatives, USA

The Center for Animal Alternatives primarily serves the animal care community of the nine campuses and three national laboratories of the University of California (UC). Its main focus is on alternatives in education (31, 32). With regard to alternatives research, the Center acts as a referral service, providing information on how best to search for the required information, but leaves the search itself to the enquirer or the local information service provider. The Center publishes a newsletter, *UC ALERT (University of California Alternatives in Education, Research and Testing)*, and lists of information resources on animal welfare and alternatives. These resource guides have recently been placed on the Web (http://www.vetmed.ucdavis.edu/Animal_Alternatives/main.htm) and, in themselves, can be considered as a database. The Center receives an average of one query a week regarding either its activities or information on alternatives.

ZEBET, Germany

The Centre for Documentation and Evaluation of Alternative Methods to Animal Experiments (ZEBET) database documents about 300 reduction, refinement or replacement alternatives in all fields of biomedicine, and contains a total of 4300 bibliographic references (33). The database is used to provide advice and information to scientists and animal welfare officers during the process of licensing applications for animal experimentation. In controversial cases, ZEBET makes an official statement to the regional authorities which may be used in court. In addition, ZEBET handles more-general queries on alternatives from all sectors of society. In total, ZEBET answered 947 queries between 1989 and 1996. ZEBET's staff members are trained in the biological sciences, as well as in search strategies for open-access data-

bases. An online connection with DIMDI, the German Institute for Documentation and Information, provides ZEBET with direct access to all important national and international biomedical databases (34, 35). A trial is in progress to offer public access to the ZEBET database through DIMDI (e-mail. zebet@bgvv.de).

Information to be Included in Databases on Alternatives

The workshop participants recognised that there is a wide spectrum of potential users of information on alternatives, including scientists in academia and industry, teachers, students, animal technicians, animal welfare officers, government bodies and regulatory authorities, pressure/lobby groups for animal welfare, and members of the general public. This wide range of users implies a correspondingly wide range of information needs, which are addressed in different ways by the various existing services.

It was generally agreed that a number of different databases and information services are needed, because they serve entirely different purposes, according to the requirements of their respective institutions (for example, Akademie für Tierschutz, ECVAM, FRAME and ZEBET) and the users of these services. It was agreed that information on the following topics is required to support the further implementation of the Three Rs: a) replacement alternatives; b) reduction alternatives; c) refinement alternatives; d) methodologies, including test protocols; e) alternatives used in education and training; f) test results (original experimental data); g) (quantitative) structure-activity relationships; h) evaluation and validation of alternative methods; i) experts and laboratories using alternative methods; j) possible sources of funding for the development of alternatives; k) regulations or guidelines on testing and quality control (national and international); and l) current projects on the development of alternative methods.

Most of the information systems represented at the workshop address one or more of these topics. The purposes and contents of these databases are defined by their respective owners. However, none of the information systems provides sufficient information on test guidelines and regulations, or on pro-

jects being undertaken in different countries. Some information providers, such as *INVITTOX* and the Akademie für Tierschutz, can provide limited information on experts working in the various fields of alternative methods, but they do not have exhaustive listings of such individuals.

Databases on the validation and evaluation of methods are valuable when planning new validation studies, for example in the selection of reference chemicals (36). The usefulness of these databases would be further enhanced if the results of validation studies could be stored in a central repository. The database currently being established at ECVAM aims to satisfy such a requirement with respect to validation studies carried out with the involvement of ECVAM.

A database of ongoing research projects related to alternative methods would be a useful resource, since it would provide an insight into the types of alternatives currently under development, and would facilitate the exchange of ideas and help to prevent duplication of effort. Such a database is being set up by the NCA for The Netherlands.

Greater attention must be given to the wide spectrum of potential users of alternatives databases, to the diversity of their information needs, and to the wide variety of information providers in this area. So far, there has been little or no feedback from various classes of users regarding the extent to which their information requirements are being satisfied. Some investigation into these questions would therefore be desirable. For this reason, it is recommended that a survey of scientists and other users of alternatives databases be undertaken, in order to determine their awareness and use of existing databases and information services, and their needs for particular types of information that are not currently being made available.

During this workshop, the discussions focused mainly on how to improve the ways in which information could be made accessible to a wide and diverse public. However, it was also recognised that, in some cases, it may be necessary to limit access to certain types of databases (for example, for databases which contain classified information, or names, addresses and other information about individuals).

It should be emphasised that the creation and continued maintenance of databases is a very labour-intensive and costly activity. The collection and evaluation of information, the accessing of special information sources, the compilation of summary data sheets, and the storage of information in a database according to well-defined loading procedures, are all activities which require considerable effort. The financial issues related to the provision of information on alternatives must not be overlooked.

Sources of information

Information which can be included in databases is usually acquired from a wide variety of sources. These include existing general bibliographic databases (for example, MEDLINE or AGRICOLA), technical reports and (when available) interim reports on projects, and information obtained directly from scientists. Some scientific journals publish, or make available, raw data that can be incorporated into factual databases.

There are several non-English language sources of information on alternative methods. A problem with these sources is that they are sometimes difficult to track down by people with no, or limited, command of the language concerned.

Special attention needs to be given to sources of information on validated and/or evaluated methods. Existing alternatives databases do not usually provide much information about the progress that has been made with the validation or implementation of the methods that they have registered. This need is being targeted by the ECVAM database on validation studies, which was mentioned previously.

Public databases, in general, lack in-house data from industry. These data can be useful in the development, evaluation and validation of alternative methods. Although, on various occasions, representatives from industry may have agreed in principle on the desirability of making such data available, this does not often happen for reasons of confidentiality. To rectify the problem, renewed efforts should be made to approach companies with requests for access to their in-house data. In this respect, an ECVAM workshop on Issues Relating to the Release of Proprietary Information and Data on the Validation of *In Vitro* Methods was held in Munich, Germany, on 9–11 May 1997. The

objective of this workshop was to determine whether companies could be encouraged to make available data which would enable third parties to validate alternative methods, by exploring the issues relating to the business value of confidential data and the value of sharing these data to improve test method validation. A report on this workshop will be published in due course.

Updating of information

The continuous increase in scientific output necessitates extensive efforts by database producers/managers to keep their products up-to-date. In this context, it should not be forgotten that updating databases containing selected and evaluated information is a skilled task, which requires well-trained staff with experience in information science. Different skills and knowledge are required for the identification and evaluation of information on different classes of alternatives (that is, reduction, refinement or replacement alternatives).

In addition to the need for frequent updating, it is also necessary to define and make known the quality criteria for the acceptance of information into the various databases, and to apply these criteria in the updating process. Only in this way will it be possible to maintain reliable databases. Further discussions on this subject are needed.

The workshop participants recognised that, for some databases, it is essential to obtain direct input from scientists and others in specific field(s) of activity. However, some participants reported difficulties in this respect.

Ways of Improving the Dissemination of Information on Alternatives

Central Reference Point on alternative methods

To increase and optimise the use of the various information services on alternative methods, it is necessary that they should be made easily accessible. In addition, information should be provided on the contents of all the different services offered, and on how to access them. One way to accomplish this objective is to create a Central Reference Point (CRP). The CRP should provide an overview of existing databases and/or infor-

mation systems on alternative methods for all classes of users. It should direct users to the appropriate information service(s) for their specific requirements. The CRP should make this information available through all possible forms of communication, including more-traditional means such as ordinary mail, telephone, fax, leaflets and CD-ROM, as well as providing access through Web sites. Although it must be emphasised that Internet access has not yet become a universal phenomenon, the CRP could also offer online facilities, including hyperlinks to databases and/or information systems which are already available through the Internet. To facilitate access, mirror sites of the CRP could be positioned at strategically placed locations worldwide (for example, in the Far East, in the USA and in Australia).

The ultimate aim of such a CRP is to improve the dissemination of information on alternatives, but it could also facilitate the exchange of information between database producers/managers. An international organisation such as ECVAM could play a significant role in setting up and maintaining a CRP. Regardless of which organisation takes on this responsibility, the requirements necessary for the maintenance of the CRP will warrant careful consideration. To define the feasibility of such a project and the best way forward, more detailed discussions are necessary. It would be desirable for this to be coordinated by a task force arising from this workshop.

Search strategies for traditional bibliographic and factual databases

The difficulties that arise when searching for information on alternatives in bibliographic databases can be due to one or more of the following: a) the information may be spread over a wide variety of information sources; b) there are many different types of alternatives (for example, mathematical models, cell culture systems, and methods that reduce animal use or minimise suffering); c) the abstracts in the database often do not contain the necessary information to show that an alternative method is under discussion in the referenced document, often due to the fact that the emphasis of scientific articles is on hypotheses, results and conclusions, rather than on the methodology used; and d) different bibliographic databases use different keywords and have different indexing criteria.

To overcome these difficulties, consideration must be given to the use of existing thesauri (that is, lists of keywords and indexing terms, which may or may not be organised according to a hierarchical system) and to the possibility of defining additional keywords related to the topic of alternative methods. The availability of a thesaurus is one of the most important prerequisites for effective searching in bibliographic databases. For example, the US NLM produced the high-quality MeSH thesaurus for MEDLINE. However, even when existing thesauri are used, some publications on alternatives are still difficult to find, and often only well-trained information specialists can retrieve the desired information.

It is therefore important to consider how the use of databases could be improved by extending the present thesauri by means of a standardised "list of preferred terms" (LPT), to be used by bibliographic and factual databases for the indexing of publications relating to alternative methods. The LPT should ideally be sufficiently extensive to facilitate any type of searching on any of the Three Rs, although it may not be possible to fully achieve this objective. Scientists publishing articles with keywords defined by the authors should be encouraged to use the terms listed in the LPT.

It is recommended that the construction of the LPT should be a further objective of a task force arising from this workshop. This task force should also coordinate the dissemination of the LPT (for example, through the Internet, by publication in journals, and by all other means available), to ensure its widest possible use. The developers and managers of international databases should be encouraged to include the LPT in their thesauri and to assign the preferred terms to existing or new information. It is clear that such a task force will have to investigate all activities which have already been initiated in this respect, and be aware of all recent developments aimed at improving online searching for information on alternatives to animal use.

The LPT will need to be in English. It will contribute to the harmonisation of: a) the identification and indexing of publications relevant to alternatives; and b) the construction of search strategies focusing on alternatives. With respect to the latter, it should also be noted that many databases and data-

base hosts provide help facilities for inexperienced users, together with a menu-driven, rather than a command-line, interface, as well as offering the option of choosing between an easy or an advanced search mode. Thus, it is possible to search certain databases with some success even without prior training. However, it may not always be possible to refine the search to the same degree as could be achieved by a trained individual possessing a high level of familiarity with the structure and indexing system of the database concerned and using the host search language to its fullest capacity. Ideally, all potential users of electronic databases should be given access to training in search techniques and search languages, for example, through courses such as those offered by AWIC, DIMDI and PREX.

Problems Pertaining to Alternatives Databases

General

Problems may be encountered in the acquisition of relevant information for the construction of alternatives databases. It is often necessary to use a variety of different sources and to exercise discrimination in the choice of material to be included. Problems experienced with some well-established databases include: a) limitation to specific sources (for example, selection of information from only a limited number of scientific journals); b) insufficient development of the thesaurus for matters specific to the Three Rs (unsatisfactory search strategies); and c) an interface that is not user-friendly. Steps can be taken to overcome these problems, for example by: a) extending the range of information sources used and incorporating new sources as they arise; b) having scientists pre-select and evaluate data before they are included in the database; c) constructing a functional thesaurus comprising highly specific and well-defined terms; and d) designing a comfortable user interface with versatile search capabilities.

Standardisation of databases

Although the phrase "standardisation of databases" may be interpreted in different ways, it is used here to refer to the "input and output" of files and keywords. It was

noted at the workshop that appropriate software could overcome some of the difficulties of standardisation. Since this type of standardisation is mainly a technical problem, it was not addressed at the workshop in any great detail.

Language problems

Another aspect of standardisation is the language in which the information is supplied. There is a need to provide information on alternative methods in English, in order to maximise access to relevant publications. It is therefore desirable for databases created in other languages to supply some core information for each record in English, to enable it to be used at an international level. At the very least, English keywords should be added to the terms used to index documents published in other languages.

Costs of using databases

Databases are used to answer scientific, practical and ethical questions. They can serve the needs of regulatory authorities, animal welfare committees, and a multitude of scientific and non-scientific users. Databases which focus on alternatives often do not operate on a commercial basis, and can be seen to offer a social benefit both inside and outside the research community. It is desirable to keep the costs of searching alternatives databases as low as possible to improve the dissemination of this type of information.

Funding of Databases on Alternative Methods

Existing databases

It was generally agreed by the workshop participants that information should be widely and easily accessible at low cost. Nevertheless, it was recognised that it is expensive to create, maintain and expand a database. Allowance must be made for the continuous updating of database hardware and software, so that new developments in technology can be exploited.

Current sources of financial support for alternatives databases include: a) governments and/or international authorities; b) animal welfare organisations; c) industry; d) universities, other institutions or specific

projects; and e) subscription and/or usage fees. Some of the information services represented at the workshop obtain support from one or more of these sources, but it cannot be assumed that they will necessarily continue to provide long-term support. Several of the services could not report a secure financial basis for continued activity in the future. The question of how to ensure the continued existence of these services requires urgent consideration by all who wish to promote alternatives to the use of laboratory animals.

Funding of a Central Reference Point

The financial basis of the proposed CRP on alternative methods would be a central issue in any discussions on the feasibility of its implementation. A detailed estimate of the costs involved will only be possible after the content, structure and services to be offered by the CRP have been clearly defined. One objective of the proposed task force should be to clarify these issues.

Conclusions and Recommendations

1. It is beneficial to have a variety of information services which address diverse information requirements.
2. It is necessary to overcome the difficulties associated with the use of different languages in different databases. There is a need to provide a minimal amount of information in English, to facilitate information retrieval on an international basis.
3. The criteria used for data acceptance should be clearly defined for each database.
4. The continuous updating of databases is important to maintain their reliability and usefulness.
5. While online access to databases on alternatives is desirable, the provision of other routes of access (such as CD-ROM and diskettes) to at least some of the information is also important.
6. There is a need for better training of users with regard to literature searching.
7. People involved in the provision of information on alternatives should be in regular contact both with each other and with scientists, to keep up-to-date with developments in the area. One solution could be to establish an e-mail list server for use by the participants of this workshop and, by invitation, others interested in developing or maintaining databases on alternative methods.
8. The setting-up and maintenance of databases is labour-intensive and expensive. Several databases and information services on alternatives do not have secure, long-term funding to ensure their continued existence and development.
9. A CRP should be created to provide information on the contents of, and means of accessing, specialised databases and/or information services on alternatives. Access to the CRP should, ideally, be free of charge.
10. To increase the usefulness of the CRP, an Internet site should be created to provide information about, and links to, individual databases. Mirror sites could be strategically located worldwide.
11. Preferably, the CRP should operate under the auspices of an international organisation (for example, ECVAM).
12. Some types of information relevant to alternatives are not available through existing services. New information systems are required on: a) laboratories and experts working in the field of alternatives; b) test guidelines and regulations; and c) ongoing projects on alternative methods being undertaken in EU Member States.
13. Appropriate measures should be taken to gain access to non-confidential data which are currently held on the in-house databases of industrial companies.
14. It is necessary to identify all potential sources of information relevant to the development and evaluation of alternative methods. The practice of some journals in making available the raw data pertaining to their published articles should be encouraged, and these data should be incorporated into alternatives databases.
15. A list of preferred terms should be defined to improve the retrieval of information on alternatives. This should be

based on a careful analysis of existing attempts to create thesauri on alternatives. The use of this terminology in scientific publications and databases should be encouraged.

16. Regular surveys should be made of the information needs of scientists and others interested in alternatives.
17. An ECVAM task force should be established to define and implement a realistic strategy for addressing the various requirements documented in this report.

Developments Since the Workshop was Held

The Second World Congress on Alternatives and Animal Use in the Life Sciences, which took place in Utrecht, The Netherlands, in October 1996, included a session on "Communication/Databases" in which a number of presentations examined some topics relating to the provision of information on alternatives. A preliminary summary of the discussions taking place at this ECVAM workshop was also presented. The abstracts from the Congress were published as a special edition of *ATLA* (37) and can also be downloaded from the Web at: <http://oslovet.veths.no/#links>.

During a lunchtime meeting convened at the Congress by Alan Goldberg (CAAT, Baltimore, MD, USA), information providers from around the world discussed possibilities for the collaboration and sharing of information, and for forming an International Database Federation. The workshop participants also met during the Congress, to discuss new developments and activities. To promote collaboration and cooperation between information providers worldwide, they invited Professor Goldberg to participate in their private e-mailing list.

An alternatives Web site has been established at the Laboratory Animal Unit, Norwegian College of Veterinary Medicine (<http://oslovet.veths.no/databases.html>). This Web site provides information about, and links to, sources of information on alternatives. Another Web site on alternatives has been established in the USA at Johns Hopkins University, with the participation of several governmental, academic and commercial organisations (<http://www.sph.jhu.edu~altweb>).

These and other developments will need to be taken into consideration in any discussions on the proposed CRP for Europe, in order to maximise the potential for collaboration and minimise unnecessary duplication of effort.

References

1. Anon. (1994). ECVAM News & Views. *ATLA* **22**, 7–11.
2. Russell, W.M.S. & Burch R.L. (1959). *The Principles of Humane Experimental Technique*, 238 pp. London: Methuen.
3. Körner, C. (1995). Welche Literatur- und Faktendatenbanken nutzen die Wissenschaftler der Schering AG insbesondere für die Suche nach Alternativmethoden? Welche Erfahrungen gibt es? In *Ersatz- und Ergänzungsmethoden zu Tierversuchen* (ed. H. Schöffl, H. Spielmann & H.A. Tritthart), pp. 274–281. Vienna: Springer-Verlag.
4. Price, D.J. deS. (1965). *Little Science, Big Science*, 118pp. New York: Columbia University Press.
5. Kolar, R. (1997). Die 3R im Internet. II. *ALTEX* **14**, 24–25.
6. Bawden, D. (1990). Information systems and databases as alternatives. *ATLA* **18**, 83–89.
7. Wexler, P. (1990). The framework of toxicology information. *Toxicology* **60**, 67–98.
8. Wexler, P. (1990). Toxicological Information Series. II. A survey of toxicological information. *Fundamental and Applied Toxicology* **14**, 649–657.
9. Münch, V. (1994). Datenbanken für die pharmazeutische Industrie. *Die Pharmazeutische Industrie* **56**, 953–957.
10. Snow, B. (1990). Online searching for alternatives to animal testing. *Online* (July), 94–97.
11. Ungar, K. (1993). *INVITTOX*: an attempt to solve some information problems in *in vitro* toxicology. *Humane Innovations and Alternatives* **7**, 540–543.
12. Huggins, J. (1994). Communication by keyword: enhanced distribution and retrieval of information about alternatives to animal testing. *In Vitro Toxicology* **7**, 369–375.
13. Ungar, K. (1994). The status of *in vitro* toxicity testing databases in Europe. In *Alternative Methods in Toxicology and the Life Sciences, Volume 11, The World Congress on Alternatives and Animal Use in the Life Sciences: Education, Research, Testing* (ed. A. Goldberg & L.F.M. van Zutphen), pp. 449–456. New York: Mary Ann Liebert.
14. Green, M.R. (1994). Public sources of *in vitro* toxicity testing data in North America. In *Alternative Methods in Toxicology and the Life Sciences, Volume 11, The World Congress on Alternatives and Animal Use in the Life Sciences: Education, Research, Testing* (ed. A. Goldberg & L.F.M. van Zutphen), pp. 457–461. New York: Mary Ann Liebert.
15. Kolar, R. & Rusche, B. (1996). The database of the Deutscher Tierschutzbund e.V. for alternatives to animal experiments. *ATLA* **24**, 336.
16. Rusche, B. & Sauer, U. (1996). Tierversuchs-

- freie Verfahren in der Ausbildung von Biologen, Medizinern und Veterinärmedizinern. In *Alternativen zu Tierexperimenten* (ed. F.P. Gruber & H. Spielmann), pp. 257–270. Berlin: Spektrum Akademischer Verlag.
17. Rusche, B. & Sauer, U. (1994). Reviewed literature databank for alternatives to animal experiments — Gelbe Liste. In *Alternatives to Animal Testing. New Ways in the Biomedical Sciences, Trends and Progress* (ed. C.A. Reinhardt), pp. 85–88. Weinheim: VCH.
 18. Larson, J. (1997). AWIC: a historical survey of significant events 1986–present, and a glimpse of the near future. *Animal Welfare Information Center Newsletter* **8**, in press.
 19. Allen, T. (1997). Animal Welfare Information Center. *Endocrine News*, **22(3)**, 15.
 20. Dubin, S. (1997). AWIC: it's not just the law, it's a good idea. *Animal Welfare Information Center Newsletter* **8**, in press.
 21. Loprieno, N. & Loprieno G. (1995). The Sixth Amendment to Council Directive 76/768/EEC and the need for developing and validating *in vitro* alternative methods for the safety evaluation of cosmetic ingredients. *In Vitro Toxicology* **8**, 291–322.
 22. Loprieno, G. (1996). The use of a factual database for the safety assessment of cosmetic ingredients. In *Alternatives To Animal Testing. Proceedings of an International Scientific Conference Organised by the European Cosmetic Industry, Brussels, Belgium, 1995* (ed. S. Lisansky, R. Macmillan & J. Dupuis), pp. 322–324. Newbury: CPL Press.
 23. Loprieno, N., Bosco, E., Boncristiani, G., Nieri, M. & Loprieno, G. (1994). The Galileo databank of toxicity testing with *in vitro* alternative methods. I. General structure. *ATLA* **22**, 20–30.
 24. Ungar, K. (1992). The INVITTOX data bank of *in vitro* techniques in toxicology. *Human and Experimental Toxicology* **11**, 151–154.
 25. Walum, E., Forsby, A., Clemedson, C. & Ekwall, B. (1996). Dynamics of validation and the evolution of new *in vitro* toxicological tests. *ATLA* **24**, 333–338.
 26. Clemedson, C. *et al.* (1996). MEIC evaluation of acute systemic toxicity. Part I. Methodology of 68 *in vitro* toxicity assays used to test the first 30 reference chemicals. *ATLA* **24**, Supplement 1, 251–272.
 27. Clemedson, C. *et al.* (1996). MEIC evaluation of acute systemic toxicity. Part II. *In vitro* results from 68 toxicity assays used to test the first 30 reference chemicals and a comparative cytotoxicity analysis. *ATLA* **24**, Supplement 1, 273–311.
 28. Anon. (1996). The NCA: a national centre. *NCA Newsletter* **3**, 2–3.
 29. van der Valk, J.B.F. & van der Kamp, M.D.O. (1996). The Netherlands Centre Alternatives to Animal Use. *ATLA* **24**, 213.
 30. Smith, A., Fosse, R., Dewhurst, D. & Smith, K. (1997). Educational simulation models in the biomedical sciences. *ILAR Journal* **38**, 23–34.
 31. Anderson, D.C. (1997). UC Center for Animal Alternatives. *European Veterinary Libraries Group Newsletter* **3**, 12–14.
 32. Hart, L.A. & Anderson, D.C. (1995). The UC Center for Animal Alternatives. In *Alternative Methods in Toxicology and the Life Sciences, Volume 11, The World Congress on Alternatives and Animal Use in the Life Sciences: Education, Research, Testing* (ed. A. Goldberg & L.F.M. van Zutphen), pp. 445–447. New York: Mary Ann Liebert.
 33. Grune-Wolff, B., Dörendahl, A., Skolik, S. & Spielmann, H. (1996). ZEBET databank and information service on alternative methods to animal experiments. *ATLA* **24**, Special Issue, 124.
 34. Grune-Wolff, B., Dörendahl, A., Skolik, S. & Spielmann, H. (1995). Welche Unterstützung können ZEBET und DIMDI Wissenschaftlern bei der Suche nach Alternativmethoden zu Tierversuchen geben? In *Ersatz- und Ergänzungsmethoden zu Tierversuchen* (ed. H. Schöffl, H. Spielmann & H.A. Tritthart), pp. 282–288. Vienna: Springer Verlag.
 35. Grune-Wolff, B., Dörendahl, A., Skolik, S. & Spielmann, H. (1996). Erfassung und Verfügbarkeit von Ersatz- und Ergänzungsmethoden bei ZEBET. *Der Tierschutzbeauftragte* **2**, 94–99.
 36. Purchase, I.F.H. (1990). An international reference chemical data bank would accelerate the development, validation and regulatory acceptance of alternative toxicology tests. *ATLA* **18**, 345–348.
 37. Anon. (1996). Second World Congress on Alternatives and Animal Use in the Life Sciences. Programme and abstracts. *ATLA* **24**, Special Issue, 349 pp.