



European  
Commission

## THE EURL ECVAM SEARCH GUIDE

# DATA RETRIEVAL PROCEDURES Basic Principles

Re-Edition



EUR 24391 EN - 2013

Joint  
Research  
Centre



**THE EURL ECVAM SEARCH GUIDE**

# DATA RETRIEVAL PROCEDURES

## Basic Principles

**Annett J. Roi, Barbara Grune**

**EDITED BY**

**Annett J. Roi, Jon Richmond**

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**T**he EURL ECVAM Search Guide (the Guide) serves a fundamental requirement, namely that, for legal, ethical and scientific reasons, any researcher planning to, or using, animals for experimental or other scientific purposes must be well-informed about the state-of-the-art of the proposed field of investigation. In particular, to satisfy the legal and ethical imperatives that animals shall only be used for research and testing if all possible alternatives are considered but found to be inadequate.

The Guide has been produced in line with the commitment of the European Commission's Joint Research Centre to improve and promote the dissemination of information on alternative approaches to animal research and testing, as required by the EU Directive 2010/63/EU on the protection of animals used for scientific purposes. Further information about the purpose, scope and context of the Guide are to be found in the preface and foreword to the first edition, included hereafter for convenience and reference.

After its first publication in May 2012, the impact of the Guide included:

- its promotion by EU Member States implementing the provisions of the EU Directive 2010/63/EU.
- inclusion of the Guide in the 2012 June/July Top 10 (4th position) of the most downloaded publications by the European Union's Bookshop
- promotion and use of the Guide within laboratory animal science training courses at universities and scientific institutions as well as at licensee training courses set up to fulfill the requirement under Articles 23 and 24 of Directive 2010/63/EU.
- distribution of the full print run, 500 printed copies, in a very short period

This re-edition represents a comprehensive update until November 2012, providing up to date advice and resources including:

- information resources as *handy* summary tables or more detailed descriptions
- thesauruses with 3Rs relevance for indexing biomedical literature databases
- search terms and their definitions
- informative and relevant contemporary examples
- and an informative bibliography

This version of the guide provides proven, contemporary, good practice data retrieval methods, approaches and procedures for scientific information supporting the 3Rs concept. The authors would welcome feedback on the relevance of the contents of the Guide, and suggestions for material to be included in future editions.

The authors wish to express, once more, their gratitude to all those involved during the development and production of the Guide. In particular, we would like to acknowledge our gratitude to Jon Richmond for his continuous support.

*Free copies* of the guide can be obtained from the Bookshop of the European Union (<http://bookshop.europa.eu>). An Internet based application will be published this year.

**Annett J. Roi**  
**Barbara Grune**  
*April 2013*

Over the last decade, driven by both scientific needs and public concern on the animal welfare and use, it has become increasingly important to actively support and accelerate the implementation of a European policy directed to the protection of animals used for experimental and other scientific purposes. The European Commission has implemented provisions of Council Directive 86/609/EEC (now revised and replaced by Directive 2010/63/EU) (1, 77) by creating the European Centre for the Validation of Alternative Methods (ECVAM) as part of its Joint Research Centre (JRC) and defining its duties in a Communication to Council and European Parliament (75). The role of ECVAM has moreover been strengthened by the new provisions of Directive 2010/63/EU (79). In addition to its core functions as the European validation centre and related activities, the dissemination of knowledge on the use and application in practise of alternative techniques has been set out as a further major objective of ECVAM.

To help achieve the latter, a decision was taken to establish and manage a publicly available database with associated user services leading to the creation of the ECVAM DataBase service on Alternative Methods to animal experimentation, the DB-ALM<sup>1</sup>. During the 4 years when online access has been provided in its current format, the service has more than 2000 registered users to the service from 75 countries covering all relevant professional profiles active in the field of alternative methods.

Many activities aimed at *disseminating Three Rs information via databases*, including raising their profile as essential scientific resources, have their origin in the ECVAM Workshop on Alternatives Databases that took place in Germany in September 1996 (4) and brought together people from organisations and/or services from both Europe and the USA involved in the provision of information on animal alternatives to discuss the current situation and whether there is the need for improvements in accessing relevant information on the Three Rs indicating a way forward. The subject turned out to be a rather complex issue for multiple reasons inherent in the various service objectives and structures on the one hand, and due to the nature of the scientific fields to be covered (replacement and refinement of animal procedures and reduction of animal use – the Three Rs applied to regulatory testing and biomedical research) on the other. Regulatory toxicity testing with particular reference to replacement methods has generally been recognised as an area for which specialised database services, as it is the current principal focus of the DB-ALM, could provide the commonly and frequently requested information reviews and/or ‘digests’ as factual information sheets based on extensive literature reviews with related sectors in support (4,10,11,16,17,20,21,74,76) as selected references. Although a fully comprehensive system is impractical, every effort has been made to develop a practical system suited to day-to-day decision making. Meanwhile, the already huge amount of the various types of data and data retrieval systems available *via* the World Wide Web has been continuously increasing: presenting so much information that efficiently searching for relevant and reliable information becomes an even more crucial challenging part of a step-wise approach to any research project.

Ethical review process has been implemented in various European countries as part of the planning, assessment and authorisation of animal testing and experiments. In addition, new and revised regulatory requirements mandate the application of the 3Rs to

determining how test requirements are to be satisfied. At present, within many of these processes information retrieval procedures and/or literature searches continue to be considered as a burden, aggravated by the difficulties of comprehensive information retrieval by an average database user who may not possess the expertise that is required to perform an efficient yet effective search in the attempt to locate relevant information on the proposed topic of study have already extensively been documented (4,10,11,16,17,20,21,74,76). The inclusion of training for students, scientists and others on data retrieval procedures has often been identified as an obstacle to progress.

It is a universal truth that the ability to find and consider relevant information is part of a sound approach for any new scientific project, and searching for the Three Rs alternatives information is an integral part of establishing the justification for generating new animal test data, and planning or evaluating any justified proposal for animal use.

The problem can be summarised as: *“How to search the best piece of 3Rs information in the endless universe of the World Wide Web that is heterogenic, constantly changing and growing without specific training?”*

To provide a solution the Commission decided, in addition to the DB-ALM, to undertake and sponsor the ECVAM Search Guide project - and this document is the product.

The project included collaboration of specialists from the German Centre for Documentation and Evaluation of Alternatives to Animal Experiments (ZEBET) of the Federal Institute for Risk Assessment (BfR) that also runs the ZEBET database (AnimAlt-ZEBET)<sup>2</sup>.

The ECVAM Search Guide enables scientists and others to navigate through the World Wide Web considering the Three Rs concept. More than that: it provides the basic elements applicable to any data retrieval procedure in biomedical sciences. It guides to find a suitable route, to select appropriate tools, and resources and will provide a means to track record of the searches. Our aim is to link various elements together to be considered during a comprehensive search and providing a guidance by following the *“Seven Golden Steps”*.

The production of the ECVAM Search Guide involved an international project advisory team composed by different professional profiles covering its major future users, such as representing the user group of scientists, industry, the ethical committee and regulatory authority, the animal welfare movement and information scientists which have assisted and contributed with precise and constructive comments to the finalisation of the Guide and/or demonstrated clearly their interest in this project and so encouraged its best completion.

**Annett J. Roi**  
**Barbara Grune**  
*February 2011*

1. DB-ALM website: <http://ecvam-dbalm.jrc.ec.europa.eu> (last access: November 2012)

2. ZEBET database (AnimALT-ZEBET) website: <http://www.dimdi.de/static/en/db/dbinfo/zt00.htm> <http://www.bfr.bund.de/cd/448> (last access: November 2012)

I write this foreword as someone involved in science for many years, and who has to find and work with information for a living. I believed that through experience I had developed sound practices and habits, and that the ECVAM Search Guide would validate my own preferences as the benchmark for others.

I was wrong.

Through my involvement in preparation of the Guide, a process driven and managed by Annett J. Roi for the European Commission in collaboration with Barbara Grune, I now realise experience, repetition and complacency had perpetuated inefficient search methods: I had confused experience with learning, and comfort for perfection.

Some say there is no substitute for experience – well, in many cases there is: it is called education, and in the course of an afternoon's study of the Guide you can learn skills better than those I acquired by 20 years of trial and error, which will serve you well in your working life.

It is sometimes said that the two hallmarks of good science are good planning before work starts and effective communication of the findings afterwards - and that the actual conduct of the experiments, the “bit in the middle”, is of lesser importance.

This is not completely true; but it does contain an element of truth.

In science good planning is essential to clearly define the specific and novel scientific objectives to be pursued; to select the most appropriate research tools; to design the programme of work; and to devise and optimise the experimental design, protocols, data acquisition and data analysis systems. All of this is conditional upon your being able to find relevant information; evaluate it; and build on your experience, analysis and insights to turn that information into knowledge and effective action.

The ECVAM Search Guide is based on the collective experience and wisdom of others familiar with the use of IT-based information systems. By providing advice on good practice and information sources it has the potential to make many of those working in the biological sciences, if they can find a few hours to master its content, more efficient and effective.

It will make you more efficient by equipping you with tried and tested searching strategies, and identifying high quality repositories of information. By reading the Guide you can learn in a few hours what it has taken many others much longer to learn (indeed which many have not learnt from experience), whilst avoiding the mistakes they made, and frustrations they encountered, along the way.

You can use what you have learned immediately, and save hours of fruitless searching each time you follow the advice given.

It will make you more effective: providing confidence that you have both found the most relevant information, and have done so in structured way that will satisfy others that you have done a good job.

Good communications skills are required to accurately yet succinctly report findings in sufficient detail to ensure that others may not only 'do what you did' but, by reproducing your study, 'see what you saw'. Equally importantly, when preparing work for publication

careful consideration has to be given to how to choose the language and keywords that ensure your findings will be easily found and read by others working in the same field.

Here again the ECVAM Search Guide is a resource which will help you with these important elements of high quality science - in addition to ensuring that all reasonable efforts are demonstrably made to replace, reduce and refine the use of animals for experimental and other scientific purposes.

We live in an age where information is plentiful and cheap. It is also of variable provenance and quality. Although you may believe it is easy to obtain information using computer-based information technology, the sheer volume of information available makes it difficult to search efficiently and effectively - that is to obtain with the minimum of effort the maximum amount of relevant information without being overwhelmed with irrelevant information.

The purpose of this Guide is to give you the information and resources to understand how to search for information on the 3Rs efficiently and effectively, and a seven-step process to search consistently and in a structured and systematic way. It is based on experience and current good practice, and represents a body of knowledge not currently available from any other single published source.

Applied in practice it will not only improve the relevance and quality of the information retrieved, but reduce the time taken to do so. Indeed, the time taken to read, learn and apply the 'seven key steps' will be repaid the first time you have to undertake such a search to support a new study.

Four points deserve special mention.

*Firstly*, the Guide explains the importance of existing value-added sources - where informed or expert input has already effectively provided some form of quality control.

*Second*, it teaches the importance not only of selecting the correct technical search terms, but also of ensuring the correct context is either predetermined or specified.

*Third*, becoming familiar with and using thesaurus terms both when searching for information, and when publishing your own work, will be time well spent.

*Fourth*, it provides concise and relevant datasheets on key sources of information.

The ECVAM Search Guide provides scientists, regulators and those involved in the ethical review and funding of animal use with an overview of contemporary good practice.

However, as the technologies evolve new and improved search tools, tips and strategies will be devised - it is hoped that those who find these even better ways to find relevant information on the 3Rs efficiently and effectively will communicate them to the authors of the Guide for consideration when future editions and updates are prepared.

**Jon Richmond**

*Home Office, United Kingdom  
September 2010*

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We also praise our other colleagues involved in defining, compiling and preparing this Guide for subsequent publication from ZEBET of the German Federal Institute for Risk Assessment as well as from the Commissions' Joint Research Centre's EURL ECVAM and, in particular, we thank Daniel Butzke who provided a new perspectives on the field of information retrieval, as well as our colleagues Amrei Schnock, Antje Dörendahl, Nora Leich, Susanne Skolik, Stephanie Spätlich, Florian Spiegel, Sebastian Spiegel and Grazia Pellegrini who worked in support.

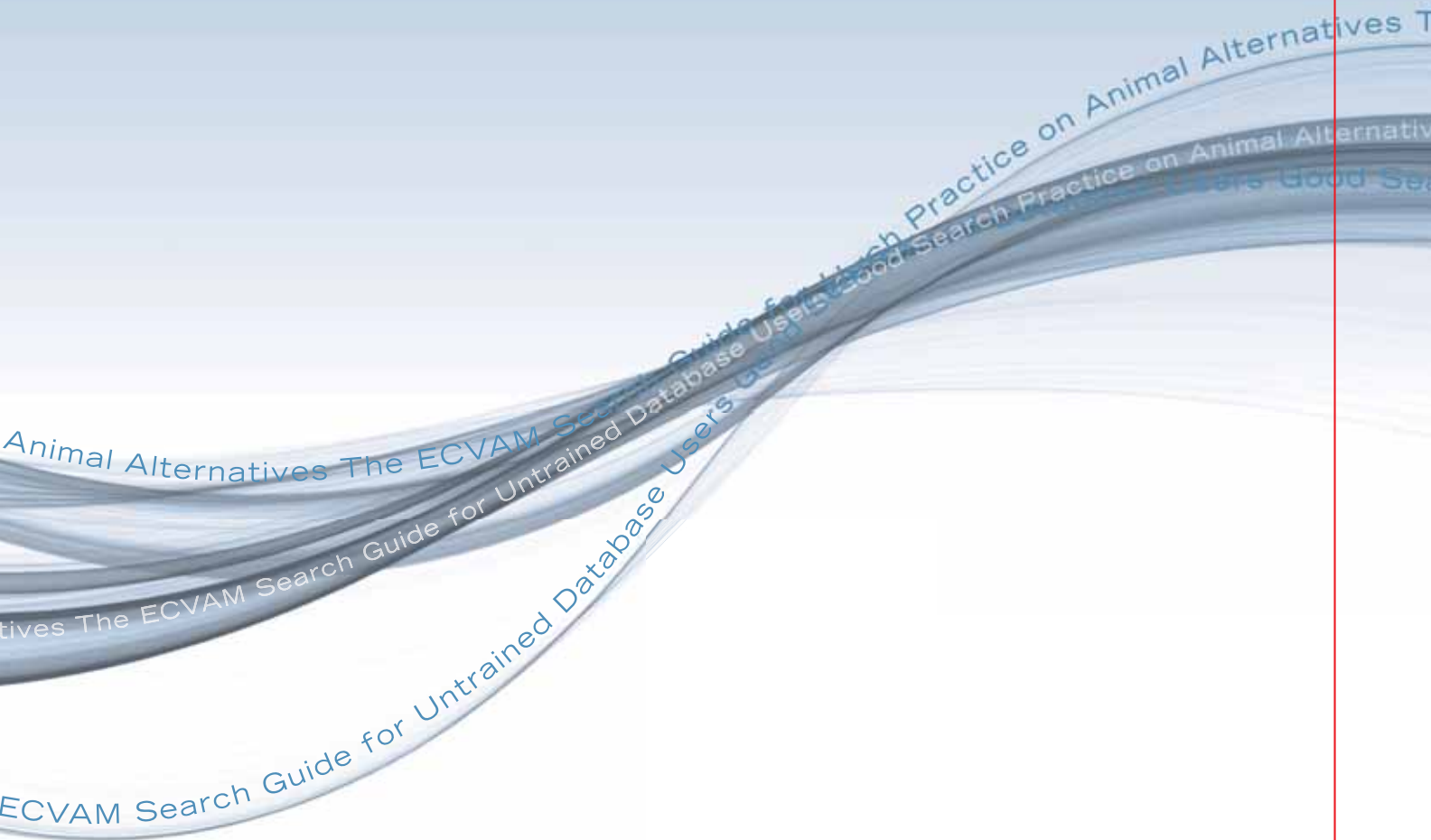
Furthermore we would like to record our gratitude to Roberto Flossi and his colleagues from the company Reggiani S.p.a. (Italy) for the generous technical assistance provided for the preparation of the Guide content as both as a "*handy handbook*" and an Internet based data retrieval system, as well as to Mare Maxwell and her colleagues from the Publication Office of the European Union for the support, helpful advice and guidance provided for the final publication of the Guide.

Lastly, but by no means least, the authors must thank the Project Advisory Team for the constructive comments and criticism provided during the course of the project development.

Annett J.Roi  
Barbara Grune  
August, 2012

# GOOD SEARCH PRACTICE

## Introduction



- The EURL ECVAM Search Guide has been specifically developed TO INFORM AND SUPPORT UNTRAINED DATABASE USERS to find high quality information on relevant alternative strategies and methods to animal experiments in an easy, yet systematic, efficient and effective way.
- This Section both introduces some of the general issues that have to be considered to plan and undertake a COMPLETE AND EFFECTIVE SEARCH FOR RELEVANT INFORMATION; and provides an overview of how the EURL ECVAM Search Guide can facilitate the PLANNING OF HIGH QUALITY BIOMEDICAL RESEARCH.
- Locating and assessing relevant findings and methodologies, and applying the information to improve scientific outputs, is a CORE COMPETENCE of those involved in the planning, conduct, communication and evaluation of scientific research.

## SEARCH PROCEDURES TO RETRIEVE RELEVANT INFORMATION ON ALTERNATIVE METHODS TO ANIMAL EXPERIMENTATION

The **European Directive** regulating the use of sentient animals for experimental and other scientific purposes requires that live animals may only be used if the specific scientific goals pursued cannot be achieved by any other means (i.e. in non-animal procedures); and when animal research is permissible the methods used must be those which minimise any justifiable suffering that may be caused (i.e. minimising both the number of animals used, and the suffering that may be caused to each animal). (1, 77)

In order to satisfy this legal requirement individual **scientists and others must be competent to determine and select the most appropriate research methods** by obtaining, evaluating and applying information on appropriate alternative, or advanced methods which replace (non-animal procedures), reduce (minimising the number of animals) and refine (minimising the suffering) animal use according to the 3Rs concept of Russell and Burch (1959). (2)

Good science and high standards of animal welfare are inseparable. Scientists' ability to identify, retrieve, evaluate and use high quality information on alternatives is critical for progress of science and animal welfare. The pool of relevant peer-reviewed information is constantly and permanently enlarging as studies are completed and findings published. (3)

The Internet enables scientists to search and display online information easily from their desks. The Internet offers access to a seemingly

unlimited amount of information on alternative methods to animal experimentation and testing.

**Even in 1996, the ECVAM Workshop "Current Status and Future Developments of Databases on Alternative Methods" estimated that at least 30,000 biomedical journals are published,** publishing more than 3,000,000 bioscience articles annually. (4) The bibliographic database MEDLINE® alone contains and provides access to over 20 million articles published in approximately 5,600 worldwide journals dating back to 1949 with a further 2,000-4,000 references being added to MEDLINE® every day. (5)

This EURL ECVAM Search Guide acknowledges both the potential of the Internet as a primary source of information to scientists, and the benefits that can be derived by learning a few simple principles and strategies to use it most effectively.

- The ability to undertake structured searches allows the retrieval of the most valuable information as quickly as possible.
- Successful Internet searches begin with a sound knowledge of the relevant high-quality information sources, the search terms most relevant to the area of work, and the ability to master the available search engines.
- **The information contained in this EURL ECVAM Search Guide will enable you to plan and conduct efficient and effective searches for relevant information both in relation to alternatives, and in other contexts.**

## WHO SHOULD USE THIS GUIDE?

The EURL ECVAM Search Guide has been developed **primarily to support untrained database users** in finding information on alternative methods in the most efficient and effective way. It is intended for use by scientists, regulators, and ethical committees involved in the planning, ethical review, authorisation and conduct of animal experiments.

The EURL ECVAM Search Guide will teach you **where and how to look for and find high-quality, relevant information on alternative methods**. You will learn exactly how to plan and conduct your search from beginning to end, using tried and tested tools and resources. Those who already have some experience will find ways of avoiding common mistakes.

By applying the insights provided in this Guide you will learn how to:

- |                                                                                     |
|-------------------------------------------------------------------------------------|
| <b>1.</b> Clearly define your information need;                                     |
| <b>2.</b> Properly identify the fundamental components of your scientific approach; |
| <b>3.</b> Identify and choose the appropriate information resources;                |
| <b>4.</b> Compile the most relevant search terms;                                   |
| <b>5.</b> Plan, conduct and document your search.                                   |

**This Guide offers practical advice to facilitate successful searches, based upon a detailed understanding of current sources of information retrieval methods.**

## HOW TO USE THIS GUIDE?

The Section Guide Road-Map of the EURL ECVAM Search Guide allows you to find your way around the Guide. The EURL ECVAM Search Guide is organised in sections and, although we recommend you to read from the beginning to end, you can select and use individual sections, chapters or datasheets, and in any order, according to your needs.

This Guide is intended to “demystify” the processes and tools which underpin successful searches by offering practical advice tailored to searching for information on alternative methods. The following main themes are covered together with supporting information:

<b>Good Search Practice</b>	sets out <b>essentials of good searching practice</b> ; introducing key search procedure elements, and explaining their significance to complete and relevant of search results; describing general features of popular search engines; and providing a manual for search terms for alternative methods.
<b>3Rs Search Procedure</b>	provides practical advice for <b>creating</b> a successful <b>3Rs search procedure</b> , structured to serve as a checklist during the planning of animal experiments.
<b>Information Resources</b>	is a repository of key current <b>3Rs information resources</b> with datasheet descriptions of each.
<b>Annex I</b>	summarises the <b>legal basis</b> of information requirements on alternative methods in the EU.
<b>Annex II</b>	contains the <b>bibliographical index</b> to key reference documents.
<b>Annex III</b>	provides a list of <b>acronyms</b> .

## SPECIAL ASPECTS OF SEARCHING INFORMATION ON ALTERNATIVE METHODS TO ANIMAL EXPERIMENTS

The aim of any systematic information search is **to collect all essential documents without retrieving any or too many which are irrelevant**. With imperfect manual searches a percentage of essential documents will be overlooked and the “hit list” may contain information which is largely unwanted and irrelevant.

Currently **no automated software package is capable of conducting the perfect information search**: the purpose of the EURL ECVAM Search Guide is to teach you to make the best use of cur-

rent resources and optimise the efficiency and effectiveness of your searches – to maximise the retrieval of relevant information, and minimise the retrieval irrelevant material.

A number of general issues are regularly encountered when planning and performing literature searches. These are discussed in more detail in the original literature. (4, 6-32, 61)

## WHERE TO FIND INFORMATION?

### Searching Scientific Databases

Established scientific factual, eg. DB-ALM and AnimALT-ZEBET, and literature databases, e.g. MEDLINE® and EMBASE, provide high-quality up-to-date systematised information on alternative methods. The best databases complement rather than duplicate the contents of others, and for that reason assuming they are interchangeable is incorrect, and **searching only one such database is usually insufficient**.

### Browsing and Searching Internet Sources

The **Internet provides access to huge amounts of information on the 3Rs** from a wide range of online sources including web-based literature, factual databases, and specialised web sites providing information on alternatives to animal studies. Added-value databases (e.g. DB-ALM, AnimALT-ZEBET and NORINA) contain both expert evaluated information and/or commentaries. Effective searches include both databases and web-sites.

There are three main problems to bear in mind: there is so much information available that searches have to be carefully planned to maximise the retrieval of that which is relevant and minimise the retrieval of that which is irrelevant; much of the **information that can be retrieved is of different levels of quality**; and the internet resources structure the information they contain in different ways, and provide different search tools.

The EURL ECVAM Search Guide will help you overcome these problems by providing you with information on the most relevant high-quality online resources, and showing how best to focus on the retrieval of only the information you need.

### Accessing the Invisible Web

It is estimated that the **Invisible Web is several orders of magnitude larger than the Surface Web**.

The term “Invisible Web” (also referred to as the “Deep Net”, “Deep Web”, or “Hidden Web”) refers to World Wide Web content that is not searchable by conventional search engines (e.g. subscription databases requiring registration), and sources containing documents in formats that are not accessible to the common search engines.

There are some freeware packages providing easier access to parts of the Invisible Web – for example Scirus, a search engine operated by the scientific publisher Elsevier.

## HOW TO FIND INFORMATION?

### Search Engines

Search engines support a range of search operators such as Boolean Operators (e.g. AND, OR, NOT), determining the scope of a search query.

The nature and functionality of search operators and the search results vary between search engines; and the same is true when search operators are used within databases.

A large number of web search engines are currently available to assist users in retrieving information, however as explained above **no single search engine accesses the entire Web**. Each search engine uses its own unique algorithm to determine the relevance of the web pages it retrieves and displays. Other product specific differences include depth-of-search, the speed at which the results are returned, and the frequency with which their indexes are refreshed.

### Next Generation of Search Engines

Semantic technology provides intelligent data retrieval interfaces. Semantic search engines go beyond merely searching for keywords in information sources. **They interpret the users request, analysing and comparing concepts** derived from the descriptors provided by the questioner, and then search taking account of predicted contexts and associations.

Semantic web technology is the enabling technology for the next generation of search engines. **They mimic specific expert knowledge, recognising networks of hierarchically grouped “concepts”**, such as subject areas relevant not only to biomedical phenomena, but to specific fields of research.

### Selection of Appropriate Search Terms

A sound search procedure for alternative methods requires the informed selection of appropriate **search terms relevant to the specific objectives of the proposed animal use, the potential methodical approaches, and 3Rs opportunities** that may be relevant.

Sometimes this can be hampered by the **lack of a standard terminology** targeting all possible alternative methods: different databases, websites and journals use different terms for material relevant to the 3Rs. Furthermore, information on alternative methods may not be indexed as such in databases – especially if the reference material did not make explicit reference to the 3Rs and alternative methods. As a result, articles may not be indexed in terms of replacement, reduction, or refinement of animal experiments – limiting the value of these words as search terms.

### Keeping up with the Flow of Information

Scientific information quickly becomes outdated, and keeping up to date with the specialist literature is a challenge facing all scientists – both with respect to information relevant to current research technologies and new scientific findings.

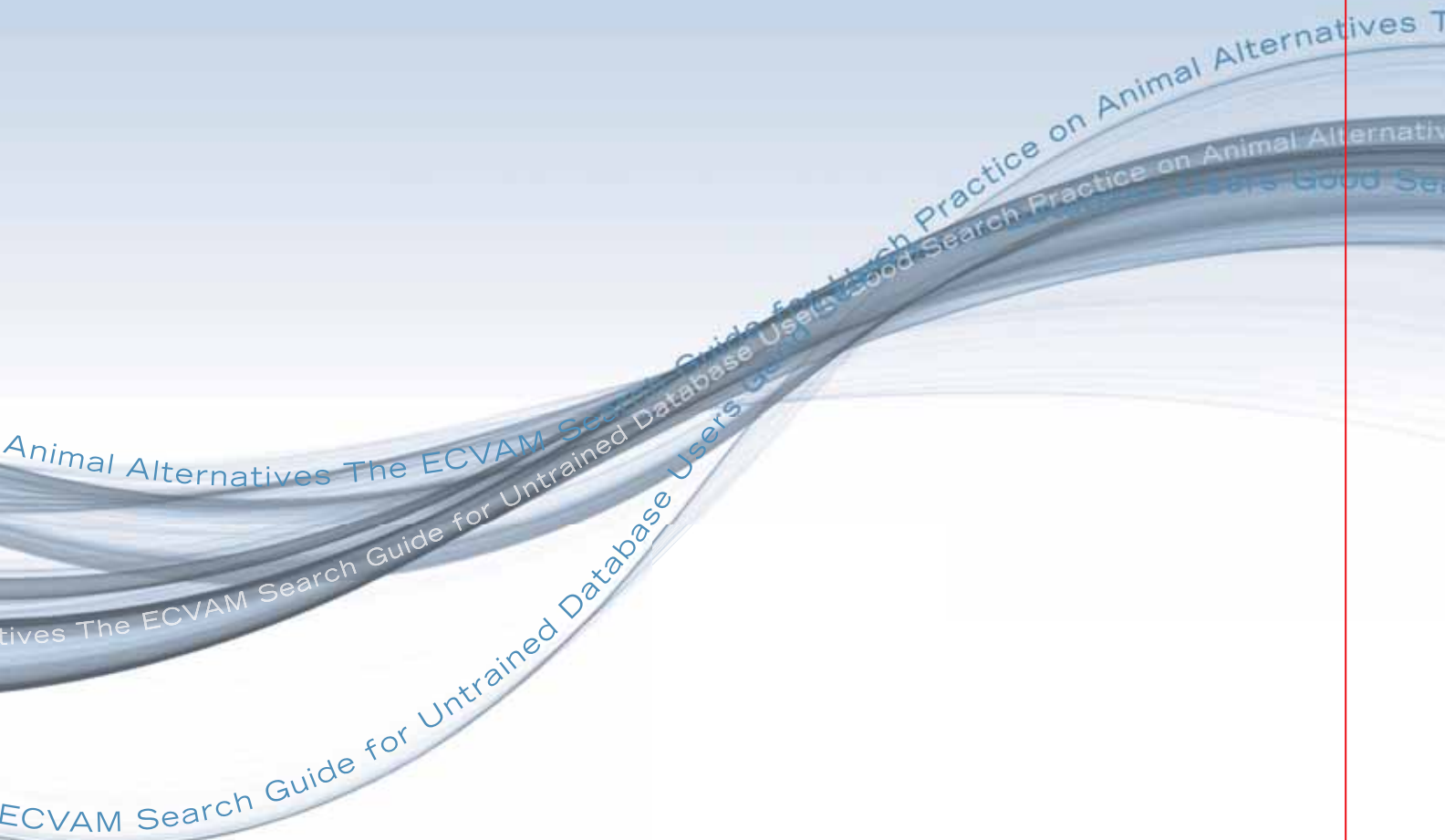
Similarly information searches soon become outdated, and have to be repeated for key elements of on-going work. Conducting quality scientific research requires teamwork and a wide range of technical competencies – including information management.

**The training of biomedical scientists in the 3Rs and how to use information resources is essential.**

In support of this objective, the EURL ECVAM Search Guide provides up to date advice on finding relevant information on the 3Rs.



# GOOD SEARCH PRACTICE Road Map



- The Road Map explains HOW TO BEST NAVIGATE AROUND THE EURL ECVAM SEARCH GUIDE.
- It shows where in the EURL ECVAM Search Guide to find detailed material on 3Rs-RELEVANT “INFORMATION RESOURCES”, “BASIC SEARCH PRINCIPLES”, “SEARCH TERMS AND THEIR USE”, AND “CREATING A 3Rs SEARCH PROCEDURE”.

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The use of wildcards to mask characters in the middle of a search term to account for spelling differences.	
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Operators expressing and defining common relationships between different pieces of information. The most familiar ones are the Boolean operators AND, OR, NOT.	
<b>Implied Boolean Symbols (+, -)</b> .....	Pag. 50
Within some search tool the Boolean operators AND and NOT may be replaced by the implied Boolean symbols + and -.	

**Context Operators (“...”, NEAR) ..... Pag. 51**

Indicating proximity relationship between search terms – for example “...” and NEAR.

**Advanced Mode Search Mask ..... Pag. 52**

If a document is represented within a database by structured metadata (for example with different files for bibliographic information on the title, author, publication year, abstract, etc) search engines generally offer the opportunity to search the individual or defined fields of metadata in a targeted fashion. The users interface may describe this as the “advanced”, “extended”, or “structured” mode.

**Field Qualifying ..... Pag. 52**

Each search box in an advanced search mask may either represent a defined subset of metadata (e.g. author name) by default, or it may allow or require field selection from a drop down menu. The number of hits can be controlled by specifying certain prerequisites, e.g. type of publication, publication year, language, etc.

**SEARCH TERMS & THEIR USE****General Considerations ..... Pag. 54****Thesauri ..... Pag. 56**

Recognised thesauri represent consensus classification of area relevant terms reached by expert review.

**Topic Defining Terms ..... Pag. 57**

Topic defining terms are the unique identifiers for the 3Rs topic: their meaning is fixed independently of the context.

**Context Dependent Terms ..... Pag. 58**

Context dependent terms are specified unambiguously only within specified contexts and refer to the field of investigations.

**Thesaurus Terms ..... Pag. 61**

Thesaurus terms are used to index database content (e.g. publications) in order to enable users to locate information relevant to a given subject.

Thesaurus terms (their meaning and context) are specified unambiguously, and their use is structured in a manner that mirrors their implied relationships (hierarchical, equivalent, or associative). Thesaurus terms are also referred to as descriptors or index terms.

**Scope Notes ..... Pag. 71**

Scope notes specify the meaning and scope of a thesaurus term.

## CREATING A 3Rs SEARCH PROCEDURE

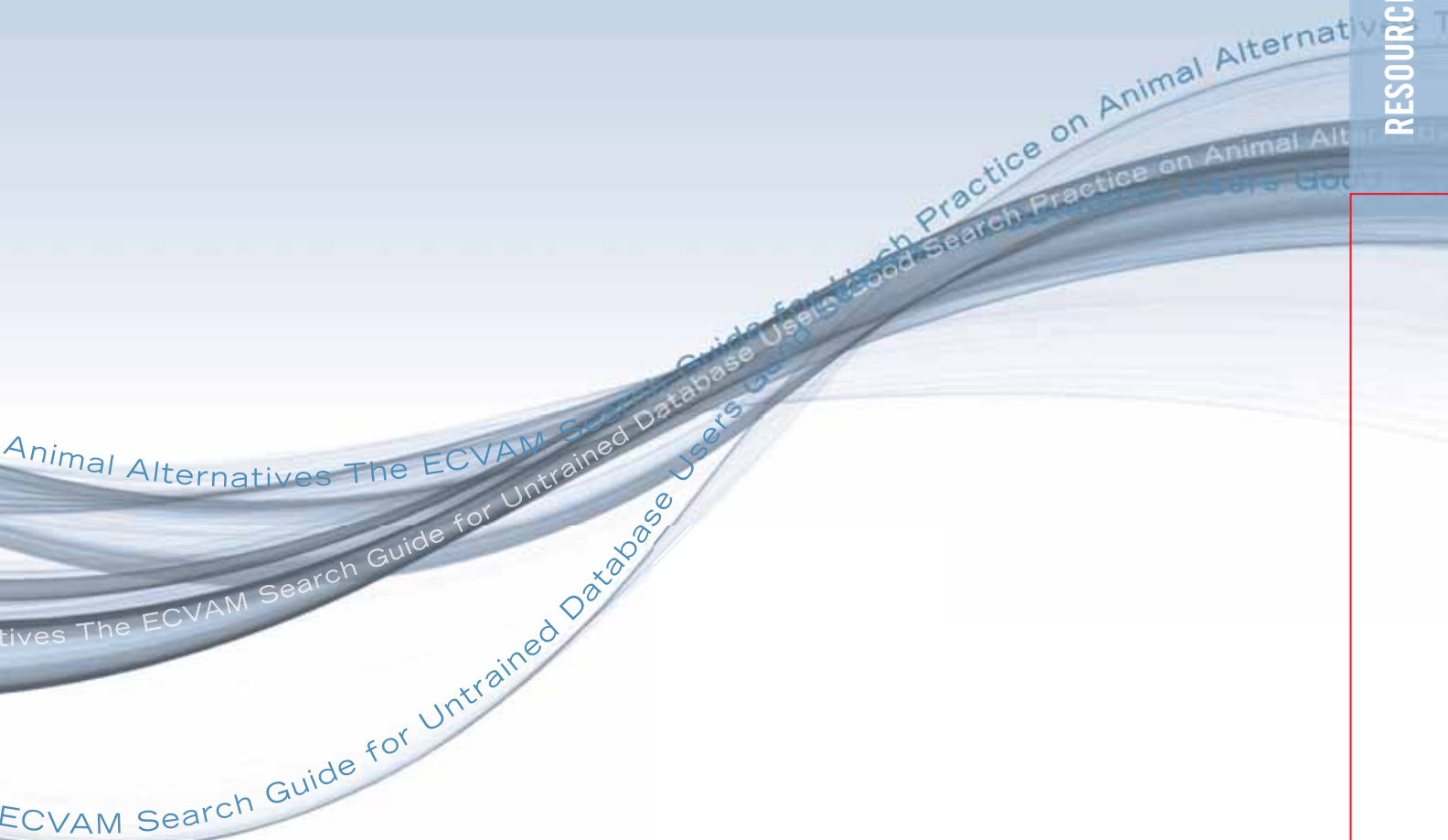
<b>The Seven Golden Steps</b> .....	Pag. 92
Key steps to successful searching are discussed in detail.	
<b>3Rs Search Procedure Checklist</b> .....	Pag. 102
The step-by-step checklist for searching information on alternative methods.	
<b>3Rs Search Procedure Examples</b> .....	Pag. 105
Worked examples of the use of the checklist method.	

## DATA SHEETS Information Resources

Information resource datasheets highlighting 3Rs key features.	
<b>Journals</b> .....	Pag. 3
Peer reviewed journals specialising in the 3Rs and laboratory animal science, and indexed by acknowledged databases such as MEDLINE and BIOSIS.	
<b>Databases</b> .....	Pag. 11
Structured collections of information organised to facilitate search and retrieval via search engines.	
<b>Meta-Databases</b> .....	Pag. 21
Collections of different information relevant to the 3Rs (e.g. bibliographic databases, patent databases, and web pages) on a single search platform.	
<b>Database Hosts</b> .....	Pag. 25
Simultaneous access to a multitude of databases relevant to the 3Rs from different providers.	
<b>Open Access Resources</b> .....	Pag. 29
Access to full-text peer-reviewed research literature relevant to the 3Rs without subscription.	
<b>Organisations and their Services</b> .....	Pag. 33
3Rs organisations providing website resources for scientists, animal welfare officers, regulatory authorities and the public. The information that can be accessed includes current activities and projects, available research funding, e-learning resources, specialist archives and databases, events calendars, links, support networks etc.	
<b>Web Search Engines</b> .....	Pag. 47
A review of widely used general and specialist web search engines, meta-web search engines, and a semantic search engine specialised in 3Rs-retrieval.	



# GOOD SEARCH PRACTICE Information Resources



- This Section introduces and explains 3Rs-RELEVANT INFORMATION RESOURCES, GROUPED ACCORDING TO THE QUALITY AND TYPE OF INFORMATION THEY CONTAIN, including:
  - journals,
  - databases,
  - meta-databases,
  - database hosts,
  - open access resources,
  - organisations websites, and
  - web search engines.
  
- The EURL ECVAM Search Guide has been developed to enable scientists and others to quickly and reliably IDENTIFY THE MOST VALUABLE INFORMATION SOURCES relevant to their specific needs for 3Rs information.

The World Wide Web constitutes an eclectic and encyclopaedic compilation of information of variable provenance and quality: indeed there are few combinations of search terms that will not yield “hits” when fed into a general web search engine (e.g. Google). That is the major problem. The concern is not that no information will be found, rather it is difficult **to construct targeted, systematic searches to obtain the most reliable and relevant high-quality information** to generate information to gain regulatory approval for a research proposal (see Annex I).

- Scientists must be able to identify and access the most suitable **information sources relevant to their specific needs for information** on alternative methods to replace, to reduce, and/or to refine a planned animal experiment or test (3Rs information).
- The EURL ECVAM Search Guide has been developed to enable scientists and others to quickly and reliably **identify the most valuable information sources related to the 3Rs** that are currently available on the web.

The EURL ECVAM Search Guide presents 3Rs information resources grouped according to the quality and type of information they contain:

<b>Journals</b>	<b>Peer reviewed journals</b> specialising in the 3Rs and laboratory animal science, and indexed by acknowledged databases such as MEDLINE, BIOSIS etc.
<b>Databases</b>	<b>Structured collections of information</b> organised to facilitate search and retrieval via search engines.
<b>Bibliographic Databases</b>	Databases containing 3Rs <b>literature references</b> to articles in professional journals, conference reports, research reports, books, newspaper articles and dissertations, etc.
<b>Added-value Databases</b>	Databases providing <b>description and evaluations</b> of original 3Rs literature based on systematic and comprehensive literature reviews. Added-value databases contain ready-to-use information.
<b>Meta-Databases</b>	<b>Collections of different information</b> relevant to the 3Rs (e.g. bibliographic databases, patent databases, and web pages) on a single search platform.
<b>Database Hosts</b>	Simultaneous access to a multitude of databases relevant to the 3Rs from <b>different providers</b> .
<b>Open Access Resources</b>	<b>Access</b> to full-text peer-reviewed research literature relevant to the 3Rs <b>without subscription</b> .
<b>Organisations and Services</b>	<b>3Rs organisations</b> providing website resources for scientists, animal welfare officers, regulatory authorities and the public. The information that can be accessed includes available research funding, e-learning resources, specialist archives and databases, events calendars, links, support networks and etc.
<b>Web Search Engines</b>	A review of widely used <b>general and specialist web search engines, meta-web search engines</b> , and a semantic search engine specialised in 3Rs-retrieval.

**Section Information Resources Inventories and Tables** lists and tabulates key 3Rs information resources. (page 33)

In addition, a datasheet is provided for each resource summarising its key features with regard the information needs set out in the volume **DATA SHEETS Information Resources** of the EURL ECVAM Search Guide.

### Diversity and Lack of Structure

A significant obstacle to efficiently retrieving information from multiple individual web resources is their diversity in content and structure and search tools and rules.

As a result **highly structured resources such as scientific abstracting and indexing databases**, hosted on the World Wide Web, are immensely powerful. (32) They contain the structured information and data required for **targeted searching**, and offer more sophisticated tools to search and manipulate this information (see Section Basic Principles).

Database information is said to be structured when specific data classes (for example author, title, source, publication date, etc.) are subdivided and captured within separate **qualified database data fields**.

This is illustrated by the processing of scientific publications into a bibliographic database such as MEDLINE. Whereas individual databases use internally consistent rules for the storage of different classes of information in different fields, different databases use different protocols and field labels.

It needs to be borne in mind that a large proportion of the most reliable and highest quality information is buried in the invisible Web (see Section on Special Aspects of Searching Information on Alternative Methods to Animal Experiments, pages 17-19), and is either not searchable by conventional web search engines and/or is only available to those who register and subscribe.

The majority of the non-subscription information available using the internet is unstructured making “advanced” targeted searches difficult, although many organisations now present their objectives, services, and information through individually designed web sites.

This is expected to become less of a problem as new generations of knowledge-based and semantic search engines offer other ways of making the best of the lack of structure inherent on the web. One example is the freely available online resource Go3R, which already provides an “**intelligent tables of contents**” feature to help make sense of vast amounts of otherwise unstructured information.

### Permanent Change

Other major challenges are posed by the rate at which information on the Web, and the means by which it can be accessed and manipulated, are **constantly changing and enlarging**.

For example, in April 2008 the beta-version of first knowledge-based search engine for 3Rs relevant contents, “Go3R”, was launched (33); in May 2008 the Windows-based search engine “Live Academic Search” was taken down (34); in July 2008 the search engine Scirus launched the beta-version of “Scirus Topic Pages” (35), and Google launched project “Knol”, software platforms where scientific experts summarise specific scientific topics, in a beta version (36).



# INFORMATION RESOURCES

## Inventories and Tables

## INVENTORIES AND TABLES

### Information Resources

- This Section provides an overview of 3Rs INFORMATION RESOURCES in the form of lists and look up tables.
- 3Rs information resources are CATEGORISED ACCORDING TO THEIR SUBJECT COVERAGE, WHETHER VALUE HAS BEEN ADDED, AND THEIR 3Rs FEATURES.
- The inventories are provided to assist in prescreening information sources and to match them to information needs.

Note: Tables are available also as handouts.

### Journals Relevant to the 3Rs Indexed by Databases and Meta-Databases

JOURNAL	Databases and Meta-Databases
Alternative Approaches to Animal Testing, AATEX	—
Alternativen zu Tierexperimenten, ALTEX	EMBASE MEDLINE PubMed SciSearch Scopus Web of Science
Alternatives to Laboratory Animals, ATLA	EMBASE MEDLINE PubMed SciSearch Scopus
Animal Technology and Welfare ATW	—
Animal Welfare Journal	CAB Abstracts EMBASE PubMed SciSearch Scopus
Institute of Laboratory Animal Resources, ILAR	AGRICOLA EMBASE MEDLINE PubMed Scopus Web of Science
Journal of Animal Science, JAS	AGRICOLA BIOSIS Previews CAB Abstracts MEDLINE PubMed Scopus Web of Science
Journal of Applied Animal Welfare Science, JAAWS	AGRICOLA BIOSIS Previews CAB Abstracts EMBASE MEDLINE PubMed SciSearch Scopus Web of Science
Lab Animal	AGRICOLA MEDLINE PubMed Scopus Web of Science
Laboratory Animals	CAB Abstracts EMBASE MEDLINE PubMed Scopus Web of Science

### Toxicology in vitro

BIOSIS Previews  
EMBASE  
MEDLINE  
PubMed  
ScienceDirect  
SciSearch  
Scopus

### Databases Categorised by their Subject Coverage

SUBJECT COVERAGE	Databases
Agriculture	AGRICOLA AGRIS BIOSIS Previews CAB Abstracts ScienceDirect SciSearch
Biomedicine	AGRICOLA AGRIS ALTBIB AnimAlt-ZEBET BIOSIS Previews CAB Abstracts EMBASE LAD MEDLINE PED ScienceDirect SciSearch
Education	HSVMA's Alternatives in Education Database NORINA
Pharmacology & Toxicology	ALTBIB AnimAlt-ZEBET BIOSIS Previews ECVAM DB-ALM EMBASE MEDLINE ScienceDirect
Veterinary Medicine	AGRICOLA AGRIS AnimAlt-ZEBET BIOSIS Previews CAB Abstracts LAD MEDLINE PED

### Databases Categorised by their Type

TYPE	Databases
<b>Added Value database</b>	AnimAlt-ZEBET ECVAM DB-ALM HSVMA's Alternatives in Education Database NORINA
<b>Bibliographic database</b>	AGRICOLA AGRIS ALTBIB BIOSIS Previews CAB Abstracts EMBASE LAD MEDLINE PED ScienceDirect SciSearch

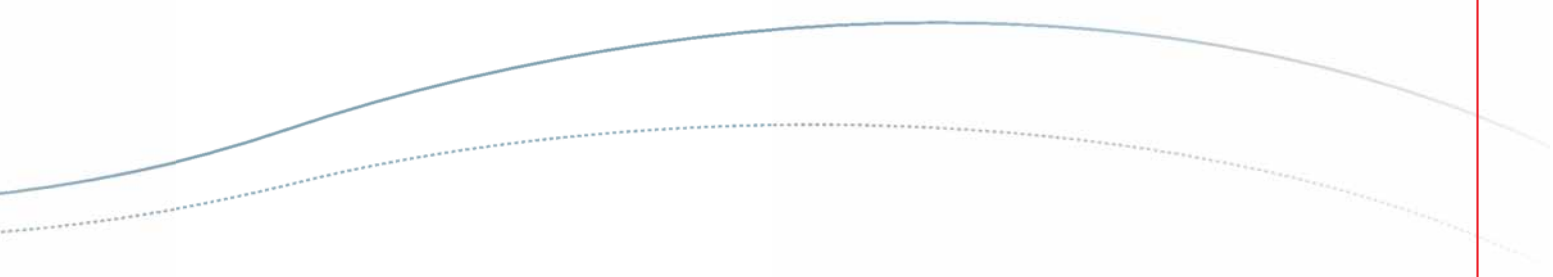
### Organisations Categorised by their Features for the 3Rs

FEATURES FOR THE 3Rs	Organisation
<b>Research Funding</b>	3Rs Res. Found. Switzerland CAAT Dr Hadwen Trust NC3Rs ZEBET
<b>Research &amp; Validation</b>	Akademie für Tierschutz CARDAM EURL ECVAM FRAME ICCVAM IIVS JSAAE ZEBET zet
<b>Education</b>	AWIC CAAT CARDAM IIVS InterNICHE UFAW
<b>Documentation &amp; Information</b>	Akademie für Tierschutz AltTox.org Altweb AWIC CAAT CARDAM Dr Hadwen Trust ECEAE ecopa EPAA ESTIV EURL ECVAM eurca FRAME HSUS ICCVAM IIVS InterNICHE IVTIP JSAAE NC3Rs NKCA UCCAA UFAW ZEBET zet

<b>Newsletter</b>	3Rs Res. Found. Switzerland Altweb AWIC CAAT Dr Hadwen Trust ECEAE ecopa ECVAM EPAA ESTIV FRAME HSUS IIVS NC3Rs NCA
<b>Communication</b>	AltTox.org ESTIV

**Organisations Categorised by their Type**

<b>TYPE</b>	<b>Organization</b>
<b>Academia</b>	Altweb CAAT JSAAE NKCA UCCAA
<b>Governmental Organisation/ European Union</b>	AWIC EURL ECVAM ICCVAM NC3Rs NKCA ZEBET
<b>Industry</b>	IVTIP
<b>Joint Organisation</b>	3Rs Res.Found. Switzerland AltTox.org ecopa EPAA
<b>Non-governmental Organisation</b>	Akademie für Tierschutz CARDAM Dr Hadwen Trust ECEAE ESTIV FRAME HSUS IIVS InterNICHE UFAW zet







THE EURL ECVAM SEARCH GUIDE

TABLE OF ORGANISATIONS CATEGORISED by their Features for the 3Rs and their Type

Organisation	Features for the 3Rs										Type			
	Research Funding	Research & Validation	Education	Documentation & Information	Newsletter	Communication	Academia	Governmental Organisation	Industry	Joint Organisation	Non-Governmental Organisation			
FRAME		•		•	•						•			
HSUS				•							•			
ICCVAM		•		•				•						
IIVS		•	•	•	•						•			
InterNICHE			•	•							•			
IVTIP				•					•					
JSAAE		•		•			•							
NC3Rs	•			•	•			•						
NKCA				•	•		•							
UCCAA				•			•							
UFAW			•	•							•			
ZEBET	•	•		•				•						
zet		•		•							•			

## THE EURL ECVAM SEARCH GUIDE

# TABLE OF DATABASE FEATURES

Database	Subject Coverage										Type			Access
	Agriculture	Biomedicine	Education	Pharmacology & Toxicology	Veterinary medicine	Bibliographic database	Added-value database	Free-of charge database						
AGRICOLA	•	•			•	•				•			•	
AGRIS	•	•			•	•				•			•	
ALTBIB		•			•	•				•			•	
AnimAlt-ZEBET		•			•	•				•			•	
BIOSIS Previews	•	•			•	•				•			•	
CAB Abstracts	•	•			•	•				•			•	
EURL ECVAM DB-ALM					•	•					•		•	
EMBASE		•			•	•				•			•	
HSVMA's Alternatives in Education Database			•								•		•	
LAD		•			•	•				•			•	
MEDLINE		•			•	•				•			•	
NORINA			•								•		•	
PED		•			•	•				•			•	
ScienceDirect	•	•			•	•							•	
SciSearch	•	•			•	•				•			•	



## THE EURL ECVAM SEARCH GUIDE

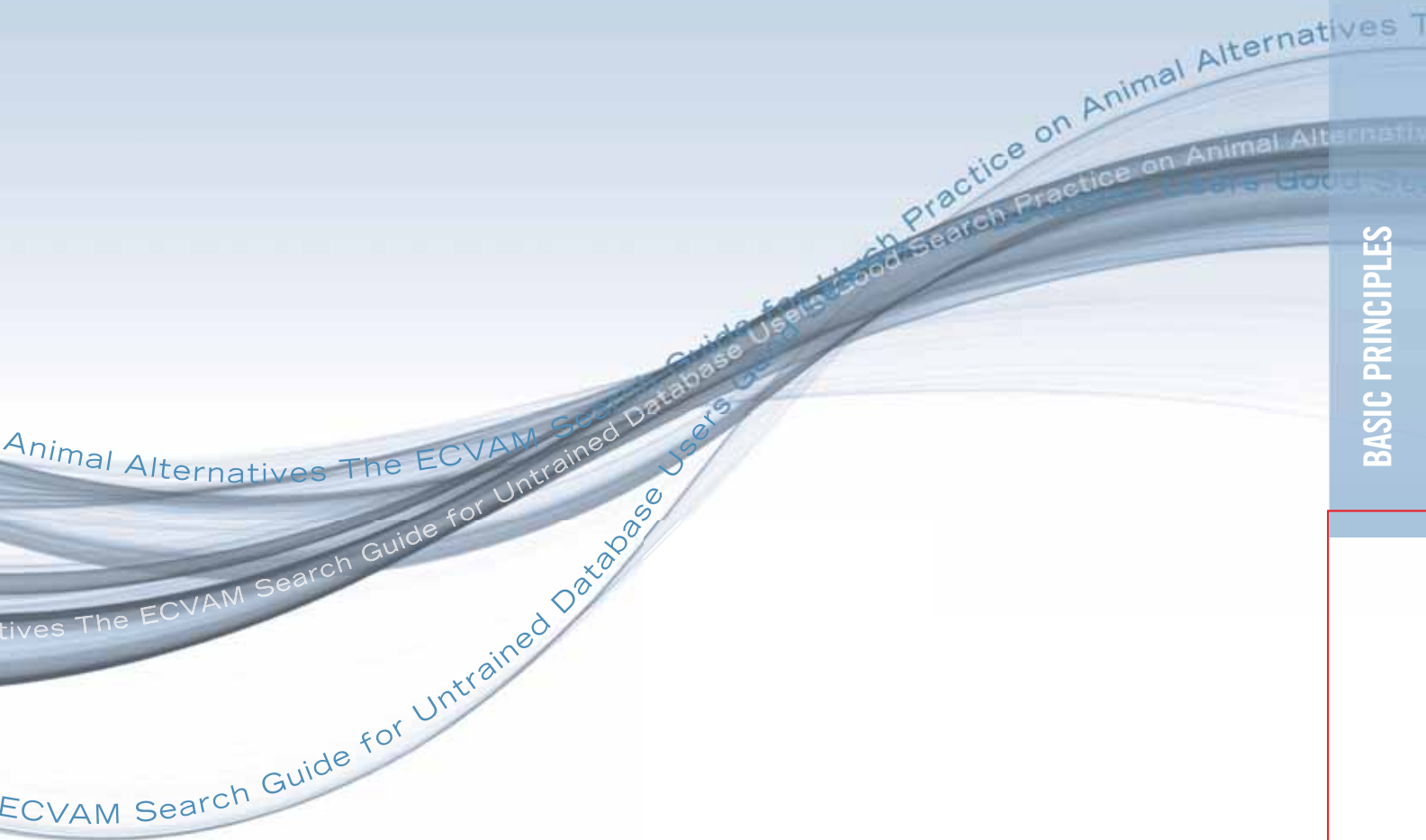
# TABLE OF JOURNALS relevant to the 3Rs indexed by Databases and Meta-Databases

Journal	Databases										Meta-Databases			
	AGRICOLA	BIOSIS Previews	CAB Abstracts	EMBASE	MEDLINE	ScienceDirect	SciSearch	PubMed	Scopus	Web of Science				
Alternative Approaches to Animal Testing, AATEX														
Alternativen zu Tierexperimenten, ALTEX				•	•		•	•	•					•
Alternatives to Laboratory Animals, ATLA				•	•		•	•	•					
Animal Technology and Welfare ATW														
Animal Welfare Journal			•	•			•	•	•					
Institute of Laboratory Animal Resources, ILAR	•			•	•				•	•				•
Journal of Animal Science, JAS	•	•			•				•					•
Journal of Applied Animal Welfare Science, JAAWS	•	•		•	•		•		•	•				•
Lab Animal	•				•				•	•				•
Laboratory Animals			•	•	•				•	•				•
Toxicology in vitro		•		•	•		•		•	•				•



# GOOD SEARCH PRACTICE

## Basic Principles



- BASIC RULES on effectively and efficiently searching for information using Internet resources are outlined in this section.
- Database or Internet searching is commonly based on the principles of BOOLEAN LOGIC (AND, OR, NOT).
- The “BASIC” SEARCH MODE, where search terms are entered in a single search box, is THE SIMPLEST BUT LEAST POWERFUL WAY TO START A SEARCH.
- The “ADVANCED” SEARCH MODE allows search queries to be stated more precisely within qualified fields (e.g. type of publication, publication year, language, etc.), and so INCREASING THE RETRIEVAL OF RELEVANT INFORMATION and decreasing the retrieval of non-relevant information.

In a matter of seconds **search engines access and interrogate many millions of documents** on the Internet and in structured databases.

To operate at this pace they use a very simple, but nonetheless very powerful search tool – namely, **index searching**. Using this technique a search engine does not scan the full text of all available documents looking for the chosen search terms; instead it consults a comprehensive index, where **extracted single terms** from the documents are pre-stored **within a look-up table**. To generate these look-up tables, software (lexical analyzers etc.) automatically scans, characterises, and catalogues original documents, storing the terms extracted from each document.

- **The search engine then prioritises the presentation of the information** found based on the occurrence of a term within a document, and the frequency of occurrence. Documents are generally placed in rank order according to the search term frequency.

Information on the position of a term within a text, (e.g. introduction, results, or discussion) can be used by search engines: this is the basis of “advanced mode” searches where queries can

be constructed in relation to a subset of data fields (for example bibliographic and metadata fields, e.g. author, title, or keywords).

- The **number of documents in a hit list**, no matter how large, does not of itself indicate the completeness of a search with respect to whether or not all relevant information has been retrieved. Some search engines identify and eliminate duplicate entries from the hit list, making it easier to review the information retrieved.
- Every database search engine or Internet search engine follows **pre-determined, but resource specific, search algorithms**. The EURL ECVAM Search Guide contains a concise survey of general features (e.g. operators, modes for searching) for each of the recommended Internet and database search engines.
- As the tools and algorithms change over time, users are advised to refer regularly to the **“search tips” section** of their favoured search engines, where product improvements are regularly summarised, to ensure they benefit from the enhanced features that may have been provided.

## SINGLE WORD SEARCH

When accessing any source of searchable online information (e.g. database, internet search engine) the default basic search mode generally provides a single **search box** into which the search terms are entered. For most queries this “basic” mode is the most comprehensive or “global” approach of searching.

However, it is a very general approach. Although relevant information may be retrieved it is all too often buried amongst the much larger quantity of irrelevant information that is also retrieved.

The simplest way to start a basic search is to **enter a single specific search term** and send the query to the processing search engine to produce a hit list of documents or sources. Generally documents are ranked and prioritised according to a pre-determined weighting factor, for example position or number of occurrences of the search term in each document.

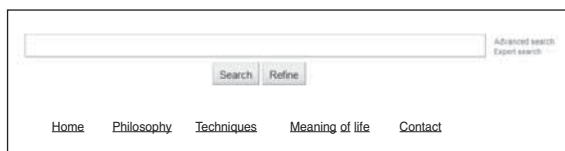


Figure 1: Example of a basic search mode mask.

### Stemming

You will sometimes find that some of the retrieved documents do not contain the search terms used, but instead include a closely related **linguistic variant** derived from the same word root. This feature is known as stemming, and more and more search engines are being equipped with an automatic algorithm to perform the necessary linguistic procedures.

**EXAMPLE** Searching for *experimentation* may show documents that instead contain the terms *experiment*, *experiments*, *experimenter*, and etc.

### Truncation

In addition to automated stemming, most search engines allow users to specify additional linguistic search options. One such tool offered by many search engines is truncation. Typically a pre-determined **wildcard** or truncation symbol is used to **replace a fixed or variable number of characters** in a search term in order to retrieve linguistic variants. Common wildcards are the symbols **\***, **?**, **\$** or **#**.

**EXAMPLE** The term *experiment?* will also show documents that contain the terms *experiment*, *experiments*, *experimenter*, and etc.

Truncating the search term without carefully selecting the most appropriate truncation point risks losing the required degree of precision required for successful searches.

**EXAMPLE** A search for *exper?* will also retrieve documents on *experts*, *experience*, *expertise*, and etc.

To minimise this danger, some search engines impose certain restrictions on the use of truncation: with some products at least three alphanumeric characters have a truncation symbol.

### Masking

A special form of truncation is **masking**. Masking allows wildcard symbols to substitute characters within a search term word: masking is one mean whereby **regional differences in spelling** can be taken into account.

**EXAMPLE** *an?sthesia* will retrieve both *anesthesia* (American English) vs. *anaesthesia* (British English)

- The use of wildcards for truncation and masking typically **increases the number of documents** retrieved, but this is generally accompanied by an increase in the less relevant material also retrieved.
- Once you have identified the search engines you prefer to use, you should go to its “**user tips**” of “frequently asked questions” section to familiarise yourself with the rules it applies to **the use of wildcard symbols**.

## MULTIPLE WORD SEARCH

When reviewing documents appearing early on the primary hit list, users should search for possible **supplementary search** terms that might be used to better differentiate that which relevant from that which appears to be irrelevant – and reasons why the search terms originally chosen were not sufficiently discriminating.

**EXAMPLE** *phage* and *display*, to describe a molecular biological method for *in vitro* production of monoclonal antibodies vs. *computer* and *display*, to describe a computer monitor.

Sometimes in order to retrieve all relevant documents all **variations or synonyms of a search term** have to be considered, e.g. *post transcriptional gene silencing* and its synonym *RNA interference*.

## Boolean Operators (AND, OR, NOT)

To capture **various textual relationships between multiple search terms within a document**, search engines allow textual relationships to be expressed in the form of operators. The most familiar of these are the **Boolean operators** AND, OR, NOT.

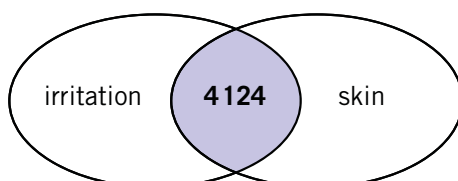
### The Operator AND

The operator **AND** is used to retrieve documents that contain both of the specified search terms anywhere in the text.

Compared to searching for the single terms, the hit list is **narrowed down** to documents only containing both terms.

When two or more search terms are simultaneously entered into the search box most by default most search engines assume and apply an AND operator.

**EXAMPLE** The combination of *irritation AND skin* will retrieve documents that mention both terms in some way, but need not necessarily focus on the endpoint “skin irritation”.



e.g. Pubmed: “irritation”	=	15 028
“skin”	=	572 123
“irritation” <b>AND</b> “skin”	=	4 124

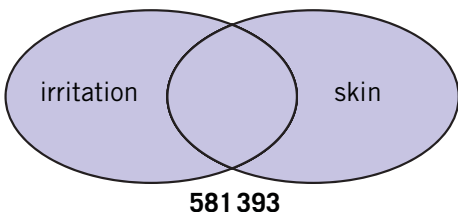
(August 28, 2012)

*Figure 2:* Subset of documents containing the terms irritation AND skin. Documents that are retrieved via a query for both terms linked by AND are indicated by purple colour.

### The Operator OR

The operator **OR** is used to retrieve documents that contain either the first or the second or both search terms anywhere in the text. The resulting **hit list is increased** by using this operator.

**EXAMPLE** OR should be used to include all synonyms of a term into the search, e.g. to find documents that mention *skin* or *dermal*.



e.g. Pubmed: "skin" = 572 123  
 "dermal" = 33 265  
 "skin" OR "dermal" = 581 393

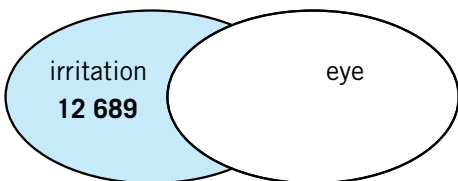
(August 28, 2012)

Figure 3: Total set of documents containing the terms skin OR dermal. Documents that are retrieved via a query for both terms linked by OR are indicated by purple colour.

### The Operator NOT

The operator **NOT** is used to retrieve documents which contain the first – but not the second - search term. Again, compared to a basic search using the same terms, the **hit list is shortened** by eliminating irrelevant information.

**EXAMPLE** The combination irritation NOT eye will exclude all documents that mention the term eye - even if a document is chiefly about skin irritation and the authors are just emphasizing the differences from eye irritation.



e.g. Pubmed: "irritation" = 15 028  
 "eye" = 284 543  
 "irritation" NOT "eye" = 12 689

(August 28, 2012)

Figure 4: Subset of documents containing the terms irritation NOT eye. Documents that are retrieved via a query for both terms linked by NOT are indicated by blue colour.

Inappropriate use of the operator NOT can result in loss of relevant information.

In contrast, inappropriate use of the OR operator may retrieve more irrelevant information.

### Implied Boolean Symbols (+, -)

With a number of internet search engines, the **Boolean operators AND and NOT can be replaced** by the implied Boolean symbols + and -.

### Boolean operators for more complex searches

Boolean operators and searches are also generally provided when search engines allow search terms to be entered in multiple boxes and/or for more than one class of data field.

**EXAMPLE** “Find web pages that have all these words” for AND.



The image shows a screenshot of the Google advanced search interface. It features a heading "Find pages with..." followed by five search options, each with a corresponding input field:

- all these words: [input field]
- this exact word or phrase: [input field]
- any of these words: [input field]
- none of these words: [input field]
- numbers ranging from: [input field] to [input field]

Figure 5: Combination of several search boxes in Google, [http://www.google.com/advanced\\_search?hl=en](http://www.google.com/advanced_search?hl=en)

### Operators to indicate Term Relations (“...”, NEAR)

The use of Boolean operators as set out above does not take account of the relative **positions of the search terms in the information being searched**. Other operators are available which allow the relative position of search terms to be taken into account.

The most **direct relationship** is where the search terms appear one after the other in the text: most search engines allow this precise relationship (where several words are effectively a single search term) to be specified by placing the relevant search terms within a single set of quotation marks.

**EXAMPLE** The query “*skin irritation*” will retrieve documents that mention this toxicological endpoint explicitly as “*skin irritation*” – but not documents where “*skin*” and “*irritation*” do not occur together.

Another way to signal that you are only interested in documents where the search terms appear in close textual proximity is to use the **context operator NEAR**, provided it is available. This operator will retrieve only documents where search terms in are separated by one or several words.

**EXAMPLE** The query *skin NEAR irritation* therefore will retrieve documents that mention *skin irritation* but will also retrieve documents that contain expressions like *irritation of the skin*, *skin or dermal irritation*, etc.

When the operator NEAR is used the maximum word gap allowed between the single search terms is generally predetermined by the search engine.

When information is represented within a database as **structured metadata** (that is when different subsets of the information is stored in different data fields; such as bibliographic information on the title, author, publication year, abstract, etc.) search engines can search this metadata in a selective, structured and systematic fashion.

The user interface to do so is sometimes called the “advanced”, extended”, or “structured” mode.



Figure 6: Advanced search mode mask of PubMed, <http://www.ncbi.nlm.nih.gov/pubmed/advanced>

### Field Qualifying

The most visually obvious difference from the “basic” mode is the simultaneous presence of **several search text boxes**.

Each search box either represents a fixed predetermined metadata field (e.g. author name, thesaurus term), or permits relevant data fields to be selected from drop-down menus. **Data field selection is also called field qualifying.**

- The number of hits can be controlled by specifying both the relevant data fields and the search terms they must contain.
- For example the author field can be used to specify a particular author, whilst the publication date field is used to simultaneously specify the year of publication of interest.
- Within an “advanced” search mode, **the quality searched for can be stated precisely**. Thus, a search for the *author Russell, WMS* will only render documents by this certain author.

**NOTE** A “basic” mode search will produce a hit list not only of documents by the author, but also documents that refer to the author (e.g. in the bibliography).

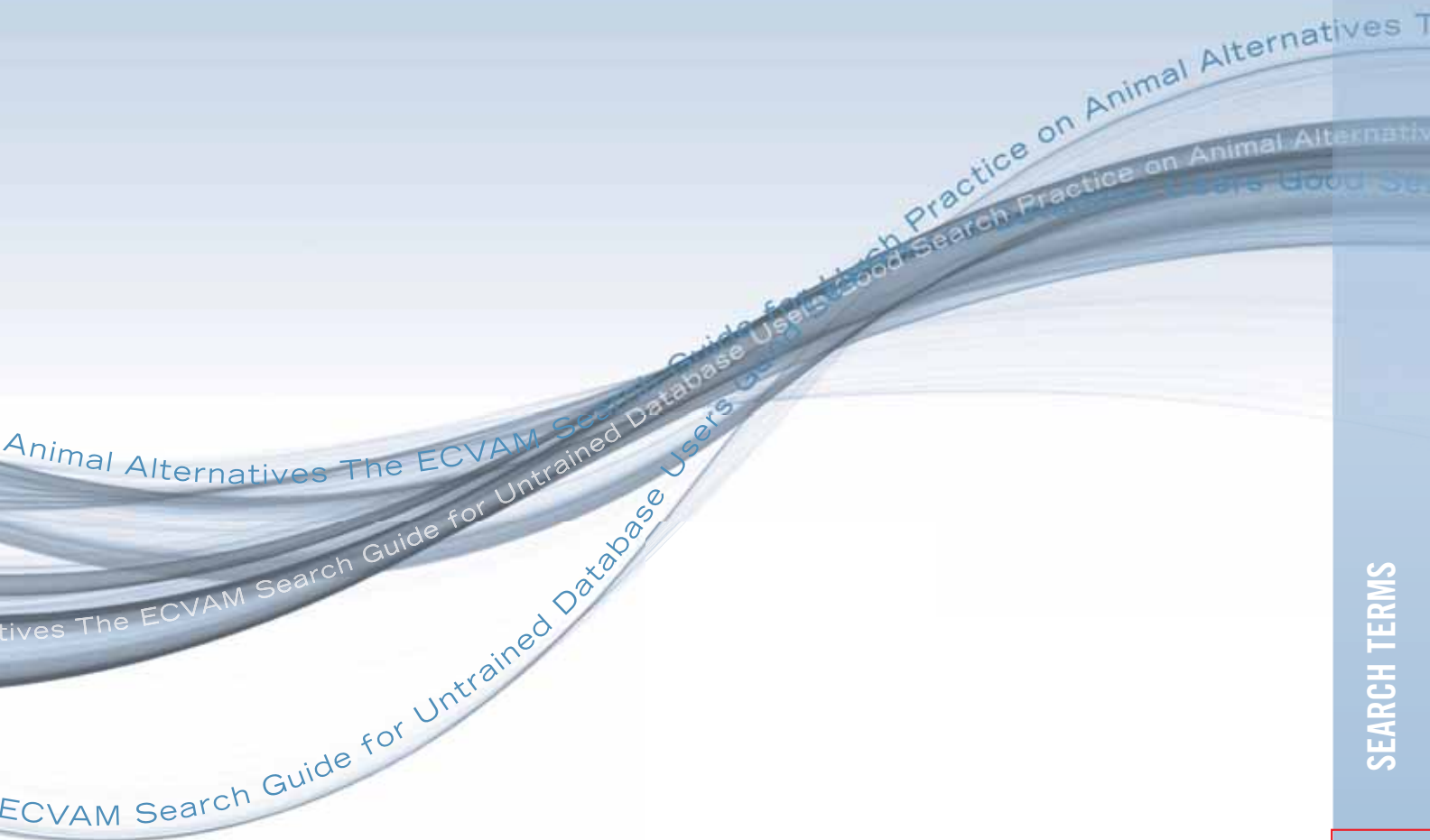
As in the “basic” mode, multiple search terms can be entered simultaneously in any specified search box, and required term relations can be defined as indicated above (Boolean and context operators, parentheses). But in addition multiple search terms also can be targeted at data contained in individual data fields.

**EXAMPLE** *Russell, WMS in author and The Principles of Humane Experimental Technique in title.*

The search boxes then can usually be linked by Boolean operators in the same manner as the single search terms.

# GOOD SEARCH PRACTICE

## Search Terms and their Use



## GENERAL CONSIDERATIONS

### Search Terms and their Use

- This Section focuses on the selection and use of SEARCH TERMS FOR ALTERNATIVE METHODS.
- In practice many scientific terms are not unambiguously specified. The solution is to UNDERSTAND HOW TO SPECIFY OR RESTRICT THE CONTEXT where relevant information will be found.
- SEARCH TERMS MUST BE RELIABLE IDENTIFIERS OF RELEVANT INFORMATION. They can be derived from relevant literature or by extracting the most appropriate terms of thesauri (descriptors or index terms).
- The EURL ECVAM Search Guide explains how to search for information on alternative methods COMBINING SEARCH TERMS APPROPRIATE FOR THE SCIENTIFIC OBJECTIVES OF A RESEARCH PROJECT AND THE 3Rs.

**Search terms are the basic building blocks** of any information search. Unfortunately, not only may search terms be applicable but they mean different things in different contexts, and their meaning and whether they are indexed may change with time.

**EXAMPLE** According to the MeSH Thesaurus of the National Library of Medicine, *cloning can mean “the formation of one or more genetically identical organisms derived by vegetative reproduction from a single cell” (cloning, organism) and also “the insertion of recombinant DNA molecules from prokaryotic and/or eukaryotic sources into a replicating vehicle...” (cloning, molecular). (37)* However, cloning is also a recognised term in computer sciences, where a clone *“is a hardware or software system that is designed to mimic another system”*. (30)

In practice **many scientific terms are not unambiguously specified** unless the context is also specified or restricted, which is why search terms will retrieve documents from other subject areas. The solution is to understand how to specify or restrict the context where relevant information will be found.

**Context specification** can be achieved in variety of ways:

- **One is to identify and then search a database dedicated to the context relevant to the information query.**

**EXAMPLE** Otherwise ambiguous terms such as *replacement, reduction and refinement* have a context specific meaning in the 3Rs-relevant databases DB-ALM of EURL ECVAM and AnimAlt-ZEBET. A comprehensive inventory of 3Rs-relevant information sources is provided in the volume "DATA SHEETS Information Resources" of the EURL ECVAM Search Guide.

- **Another way is to use terms from an agreed context specific controlled vocabulary defined in a thesaurus.**

A thesaurus is a compilation of relevant terms (descriptors or index terms) for a given “domain of knowledge”. Being context specific the meaning and scope of thesaurus terms are specified unambiguously. With the thesaurus they are or can be arranged to reflect their logical relationship (hierarchical, equivalent, or associative).

One of the most comprehensive thesauri in the biomedical field is the MeSH (Medical Subject Headings) from the US National Library of Medicine (NLM). The MeSH, and a number of other widely used controlled vocabularies (EMTREE, CAB Thesaurus etc.), are described in detail hereafter (see pages 62-63).

- **Context specification is also possible by combining** within a single search otherwise ambiguous search terms with **topic defining search terms** (see below) using Boolean search operators (see Section Basic Search Principles, page 49).

**EXAMPLE** The scope of a term like *replacement* is clearly restricted by a combination (AND) with the topic defining term *animal experimentation*.

The next sections include a structured list of suggested search terms relevant to the 3Rs, including common 3Rs topic defining terms (see page 64 f.f.)

Alternatively you can use free online tools to extract supplementary discriminating search terms from abstracts.

## THESAURI WITH RELEVANCE TO THE 3RS PRINCIPLE

This section provides essential information about four major **thesauri that contain 3Rs-relevant terms** such as *animal testing alternatives*. Thesaurus terms are widely used to index database content in order to enable informed users to easily locate information relevant to a given subject.

New terms are constantly considered and added as necessary as they appear in the literature, and integrated with the existing vocabulary. Importantly **thesauri also mirror the logical relationship between single terms**. This may be a hierarchical one, e.g. when several specific terms are merged under a broad “umbrella” term.

Such “**umbrella**” terms themselves can be grouped under even broader “umbrellas”, thus producing taxonomical **tree structures** with the narrowest term at the end of branches and the most universal ones at the top.

**EXAMPLE** The MeSH “umbrella” term *animal experimentation* encompasses the term *animal use alternatives* (see figure 1).

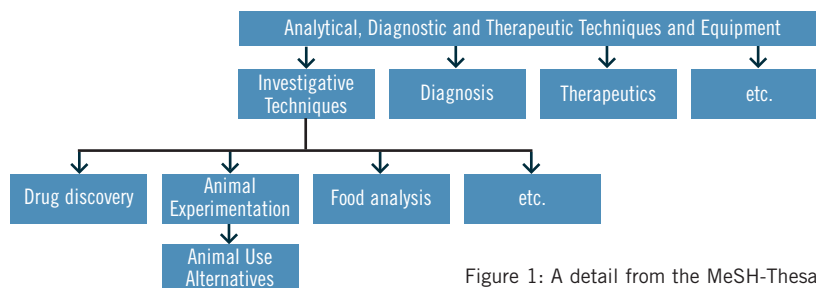


Figure 1: A detail from the MeSH-Thesaurus (2012) leading to the MESH-term *animal use alternatives* is shown. (37)

In addition, a thesaurus may automatically **link single terms to pre-defined synonyms**. Since synonyms have the same or nearly the same meaning they add to the versatility and power of searches based on thesaurus terms.

**EXAMPLE** *post-transcriptional gene silencing, co-suppression, RNA silencing* are synonyms for the MESH-term *RNA interference*.

Using 3Rs-relevant **thesaurus-derived terms in an advanced mode** query (see Section Basic Search Principles, page 45) will retrieve documents that have been assigned to the respective headings by professional indexing systems. For example, in July 2012 the search term *animal use alternatives* yielded ~ 2,550 3Rs-related documents in PubMed. Such relatively non-specific list of relevant documents can then be made shorter and more specific by then searching for specific alternatives by using relevant supplementary search terms.

To experience the full potential of MeSH-terms **PubMed provides the option to search the MeSH Database** (<http://www.ncbi.nlm.nih.gov/mesh>, Accessed July 24, 2012). (38)

This identifies the most appropriate MeSH terms for the topic of interest, and then uses these to search PubMed.

In practice most initial candidate search terms are not derived from a controlled vocabulary; they are generally derived from what the user knows about relevant literature.

- This informal selection procedure inevitably selected terms, that as far as efficiency and effectiveness are concerned, are much less useful than the more systematic approach described before.
- A better approach is to spend some time considering the possible limitations of your intuitive candidate search terms, e.g. scope, breadth, ambiguity etc.
- The best approach is to identify and use the correct thesaurus terms.

### 3RS SEARCH TERM CATEGORIES - A PROPOSAL

In searching full-text documents the scope of an ambiguous term is largely determined by the contexts in which it might be used. As advised before, **the scope of search terms can be restricted by the addition of topic specific search terms.**

The EURL ECVAM Search Guide approach is to give you the ability to use the available technology so that searches for key words can always be done in a way where you can also define the context in which the keywords should be used for the purposes of your information search.

#### Topic Defining Terms - Topic Definers

The additional terms that can best be combined with any given ambiguous search term are genuinely selected for their **scope/topic defining power.**

**EXAMPLE** From the 3Rs perspective, search terms such as *animal testing alternatives* or *animal use refinement* are consistently powerful topic definers - largely because they are terms used by many thesauri.

In some cases appropriate **topic definers can be derived from terms frequently cited in key publications** for a scientific area (38); this is especially true of recently introduced technical terms, e.g. *Gene chips* for DNA microarrays or *dendrimers* for certain nanostructures.

There are some topics where **even the names of frequently cited authors can be topic defining.** That's why "*Russell and Burch*" is included in the proposed list of search terms (see hereafter).

In the majority of cases, however, no unique or definitive terminology has been established, and defining power lies largely in unique **combinations of related terms**, e.g. searching for the combination of

*replacement, reduction and refinement* in any document. In practice most topic definers are complex terms like *animal use alternatives*.

**The purpose of topic definers is to optimise the retrieval of relevant documents** - provided that the author of a document also had the 3Rs principle in mind and used 3Rs-specific terminology. If a 3Rs-relevant document does not contain such topic specific terminology it will not be retrieved via employment of a topic definer like *humane endpoints*: it may nevertheless be retrieved from value-added database where the content is classified by relevant expert reviewers.

**Alternatively combining several more or less unspecific terms may target some of this “hidden” information**, e.g. a combination of *in vitro, toxicology and testing*. Combinations like this can only be properly designed by scientists who are already familiar with the relevant scientific areas and not by trial and error by those who are not.

### Context Dependent Terms

**Terms that do not unambiguously belong within a single specific topic are sometimes called context dependent terms.**

**EXAMPLE** The ambiguous term *replacement*, for example, needs to be placed in context to limit its range to the field of the 3Rs.

**Context dependent terms may be further classified according to their breadth.** The breadth of a term is equated to its hierarchical position within a thesaurus - the broader terms are located at the higher level (see before). In the information retrieval scheme developed for the EURL ECVAM Search Guide, the broader terms, such as *toxicology*, are pooled within the higher category *area of expertise*. *Objectives* or *subjects*, like *risk assessment* or *pharmacokinetics*, form middle category, and the lowest categories list the narrowest terms such as *tissue equivalent*.

The most specific candidate search terms for a given subject, e.g. a specific method, organ, or substance, have to be selected by the user who is searching for information about a specific alternative method to substitute for or refine a planned animal experiment (see Section The Seven Golden Steps page 92).

The **proposed classification of terms** is not of itself constitute a thesaurus; rather it reflects inherent differences in the breadth and specificity of different classes of search terms (38).

- **Broad terms** yield the largest document hit lists, but on their own will include an unacceptably large number of documents irrelevant to a specific request.
- The more **specific or narrow a search term** is, the more relevant the hit list is likely to be: but the risk of missing relevant documents is high. For example a search for *dermal toxicity* may miss documents that use the equivalent term *skin toxicity*.

### Suggestions for Topic Definers and Context Dependent Terms

**Key topic definers and context dependent terms are presented in alphabetical order in the list of categorised terms according to the 3Rs principle** (pages 65-68). These terms have been derived from published search term compilation relevant to the 3Rs principle (64-68).

The list of search terms is not meant to be exhaustive, and does not cover synonyms and inflections in detail. The listed variant of a term is based upon frequency of use. Nevertheless, other variants (number, inflection, spelling differences, etc.) also have to be considered when planning a search.

Search terms that represent **terms from recognised thesauri** are marked by an asterisk. These may be used to target documents in value added databases as appropriate, e.g. *animal testing alternatives* to retrieve all documents that have been linked to this category by expert reviewers (see before).

**Terms accompanied by a scope note** are marked by two asterisks. Scope notes define the context of a given term (see examples for *cloning* above). Corresponding full text scope notes and the term spellings are recorded in the section: Selected Terms with Definitions (pages 70-89).

Thus, Section: Search Terms and their Use (page 54) provides a systematic basis practical framework for efficient and effective advanced searches.



- This Section introduces and explains the four major THESAURI CONTAINING SPECIFIC 3Rs RELEVANT TERMS:

CAB THESAURUS of CAB Abstracts (UK)

EMTREE Thesaurus of Elsevier B. V. (NL)

MeSH (Medical Subject Headings) Thesaurus of the United States National Library of Medicine (USA)

NAL THESAURUS of the National Agricultural Library (USA)

- Thesauri are designed for INDEXING AND SEARCHING DATABASE CONTENTS. A thesaurus supplies a vocabulary as well as a classification system of terms relevant to a given DOMAIN OF KNOWLEDGE.
- THESAURUS TERMS are arranged in a manner that mirrors their LOGICAL RELATIONSHIP (HIERARCHICAL, EQUIVALENT OR ASSOCIATIVE). In a hierarchical thesaurus narrower terms are grouped under broader terms. Thesaurus terms are also called INDEX TERMS OR DESCRIPTORS; many of them have a scope note, which can be a definition of the term or a comment.

NOTE: Thesaurus terms do not necessarily correspond to the key words given by authors.

### CAB Thesaurus

<b>Producer</b>	CAB Abstracts
<b>Address</b>	CAB International Head Office Nosworthy Way Wallingford Oxfordshire OX10 8DE UK Tel: + 44 (0)1491 83 21 11 Fax: + 44 (0)1491 83 35 08 Email: enquiries@cabi.org http://www.cabi.org
<b>Access</b>	http://www.cabi.org/cabthesaurus/
<b>Fees</b>	Free of charge

#### Features for the 3Rs

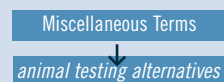
The CAB Thesaurus is a controlled and polyhierarchically structured vocabulary (~ 98.500 preferred terms in 2011) that is used for indexing the **CAB Abstracts database**, **AGRICOLA databases** and others. One key topic is veterinary medicine. The current version of the CAB Thesaurus was released in February 2010. The CAB Thesaurus provides a range of terms and their synonyms that can be employed within a search for 3Rs relevant documents. Additionally, one **specific 3Rs topic defining term** is embedded in the system:

- *Animal testing alternatives*

**Scope Note:** Scope note is not assigned.

**History Note:** This term was added to the CAB Thesaurus in 1990.

#### Tree structure:



### EMTREE Thesaurus

<b>Producer</b>	Elsevier B. V.
<b>Address</b>	Elsevier E-Helpdesk P.O. Box 211 1000 AE Amsterdam THE NETHERLANDS Tel: + 31 20 485 3767 Fax: + 31 20 485 3739 E-mail: niEMBASEinfo@elsevier.com http://www.info.embase.com/
<b>Access</b>	http://www.embase.com
<b>Fees</b>	Fee based

#### Features for the 3Rs

The EMTREE Thesaurus is a controlled and polyhierarchically structured vocabulary integrated into Elsevier's databases **EMBASE** and **EMBASE Classic**. The hierarchical structure includes all MeSH terms as main terms or synonyms. In 2012, EMTREE comprised ~ 57.000 preferred terms and ~ 235.000 synonyms. A main topic is pharmaceuticals (~144.000 drug synonyms). EMTREE is updated annually. EMTREE terms and their synonyms can be employed within a search for 3Rs-relevant documents. Additionally, one **specific 3Rs topic defining term** is provided:

- *Animal testing alternative*

**Scope Note:** Scope note is not assigned.

**History Note:** This term was added to EMTREE in 2002.

#### Tree structure:



#### Synonyms:

- animal testing alternatives
- animal use alternatives

**Available from** <http://www.cabi.org/cabthesaurus/>  
**Accessed** July 24, 2012

**Available from** <http://www.embase.com>  
**Accessed** July 24, 2012

**MeSH (Medical Subject Headings) Thesaurus**

**Producer** United States National Library of Medicine (NLM)

**Address** Medical Subject Headings  
National Library of Medicine  
6701 Democracy Blvd  
Bethesda, MD 20894-4879  
Tel: + 1 301 496 1495  
Fax: + 1 301 402 2002  
Email: nelson@nlm.nih.gov

**Access** <http://www.nlm.nih.gov/mesh/>

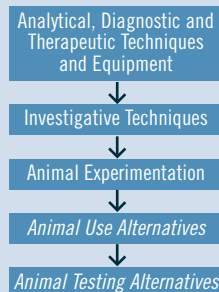
**Fees** Free of charge

**Features for the 3Rs**

The Medical Subject Headings Thesaurus (MeSH) is a controlled and polyhierarchically structured vocabulary (~26.142 terms; ~ 177.000 synonyms in 2011) used to index articles in the biomedical journals covered by the **MEDLINE database**. It is also used to catalogue NLM's own holdings. MeSH is updated weekly. MeSH provides a range of keywords and synonyms (entry terms) that can be employed within a search for 3Rs-relevant documents. Additionally, **two specific 3Rs-topic defining terms** are provided:

- *Animal testing alternatives*  
**Scope Note:** Procedures, such as tissue culture techniques; mathematical models; etc., when used or advocated for use in place of the use of animals in research or diagnostic laboratories.  
**History Note:** This keyword was added to MeSH in 1985.
- *Animal use alternatives*  
**Scope Note:** Alternatives to the use of animals in research, testing, and education. The alternatives may include reduction in the number of animals used, replacement of animals with a non-animal model or with animals of a species lower phylogenetically, or refinement of methods to minimize pain and distress of animals used.  
**History Note:** This keyword was added to MeSH in 2001.

**Tree structure:**



**Available from** <http://www.nlm.nih.gov/mesh/>  
**Accessed** July 24, 2012

**NAL Thesaurus, NALT**

**Producer** National Agricultural Library (NAL)

**Address** National Agricultural Library  
c/o Lori Finch, Thesaurus Coordinator  
10301 Baltimore Ave  
Beltsville, MD 20705  
USA  
Tel: +1 301 504 6853  
Fax: + 1 301 504 5213  
NAL.Thesaurus@ars.usda.gov

**Access** <http://agclass.nal.usda.gov/agt/agt.shtml>

**Fees** Free of charge

**Features for the 3Rs**

The NAL Thesaurus (NALT) is the controlled and polyhierarchically structured vocabulary (~ 49.000 preferred terms in 2012) of the U.S. National Agricultural Library used as a supplement to the CAB Abstract thesaurus which indexes agricultural information within the **AGRICOLA database**. The NALT covers terminology in biological, physical, and social sciences. The majority of the terms are derived from biological nomenclature.

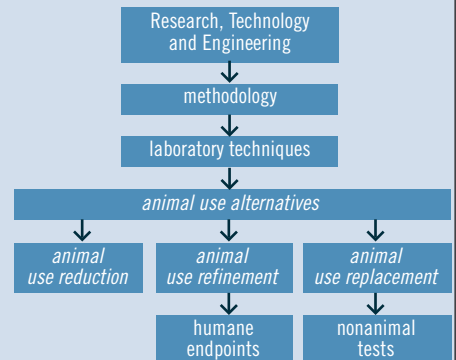
The NAL Thesaurus is updated annually. The NALT comprises several terms and their synonyms in a microthesaurus for animal use alternatives that can be employed within a search for 3Rs-relevant documents.  
<http://www.nal.usda.gov/awic/alternatives/alternativeanimalusetheasaurus.htm>

**Several specific 3Rs-topic defining terms** are provided:

- *animal use alternatives*
- *animal use reduction*
- *animal use refinement*
- *animal use replacement*

**Scope Note:** Scope notes are not assigned.

**Tree structure:**



**Available from** <http://agclass.nal.usda.gov/agt/agt.shtml>  
**Accessed** July 24, 2012

- This Section provides a compilation of search terms as an exemplary LIST OF SELECTED TERMS PARTICULARLY RELEVANT TO THE 3Rs PRINCIPLE based on a systematic review of relevant publications. It is a rich source of 3Rs search terms that can be used in any 3Rs information search.
- Search terms are categorised into TWO MAJOR GROUPS:
  - TOPIC DEFINING TERMS; listed according to their value as unique identifiers of the 3Rs topic
  - CONTEXT DEPENDENT TERMS referring to specific area of expertise, objectives and subjects.
- CONTEXT DEPENDENT TERMS are further classified according to their breadth:
  - VERY BROAD TERMS will on their own produce very lengthy, complex and non-uniform hit lists containing many irrelevant documents.
  - VERY NARROW TERMS on their own may miss many relevant documents.
- The scope of an ambiguous, CONTEXT DEPENDENT SEARCH TERM in a query can be defined and restricted by COMBINING it WITH unambiguous, TOPIC DEFINING TERMS.

## LIST OF CATEGORISED SEARCH TERMS RELEVANT TO THE 3RS PRINCIPLE

**3Rs Topic Definer***(in alphabetical order)*

3R Principle  
3Rs

**A** alternatives to animal testing  
animal experiments\*\*  
animal experimentation\*\*  
animal models\*\*  
animal research  
animal rights\*\*  
animal science\*  
animal testing  
animal testing alternatives\*\*  
animal testing reduction\*  
animal testing refinement\*  
animal testing replacement\*  
animal use alternatives\*\*  
animal use reduction\*  
animal use refinement\*  
animal use replacement\*  
animal welfare\*\*  
animal wellbeing\*  
animals\*\*

**B** bioethical issues\*\*  
bioethics\*\*

**E** ethics\*\*  
experimental animal\*  
experimental animal welfare\*

**H** humane endpoints\*\*  
humane experimentation  
humane research

**L** laboratory animal science\*\*  
laboratory animals\*\*

**R** reduction alternatives  
refinement alternatives  
replacement alternatives  
Russell and Burch

**T** three Rs

**BROAD context dependent terms  
referring to specific areas of expertise***(in alphabetical order)*

**A** animal diseases\*  
animal health\*  
animal production\*

**B** biochemistry\*\*  
bioinformatics\*\*  
biophysics\*\*

**C** cell biology\*  
chemistry\*\*

**E** education\*\*

**F** food hygiene\*

**G** genetics\*\*

**I** immunology\*

**M** microbiology\*\*  
molecular biology\*\*

**N** neurobiology\*\*  
neurology\*\*  
nutritional sciences\*\*

**O** oncology\*

**P** parasitology\*\*  
pharmacology\*\*  
pharmacy\*\*  
physiology\*\*

**R** regulations\*

**T** toxicology\*\*

### Context dependent terms of MEAN BREADTH referencing research objectives and subjects

(in alphabetical order)

- |          |                                                                                                                                                                                                                                        |          |                                                                                                                                                                                                            |
|----------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>A</b> | ADME<br>agents<br>alternatives<br>alternative procedure<br>analysis**<br>animal behaviour*<br>animal care*<br>animal conditions<br>animal handling*<br>animal husbandry**<br>animal use<br>artificial organs**<br>assay**<br>autopsy** | <b>L</b> | licensing*<br>licensure**                                                                                                                                                                                  |
| <b>B</b> | bioassay*<br>biological markers**<br>biological agents**<br>biopsy**                                                                                                                                                                   | <b>M</b> | metabolism**<br>methodology*<br>methods*<br>models*                                                                                                                                                        |
| <b>C</b> | cadaver**<br>capture of animals*<br>case study*<br>chemical analysis*<br>chemical treatment*<br>chemicals*<br>computer*<br>cosmetics**                                                                                                 | <b>N</b> | natural products*<br>nutrition*                                                                                                                                                                            |
| <b>D</b> | diagnosis**<br>diagnostic techniques*<br>diagnostics<br>disease surveys*<br>drug evaluation**<br>drug screening*<br>drugs**                                                                                                            | <b>O</b> | organ*<br>organelles**                                                                                                                                                                                     |
| <b>E</b> | endpoints*<br>enrichment*<br>evaluation*<br>experimental design*<br>ex vivo study*                                                                                                                                                     | <b>P</b> | pathogens**<br>pharmaceuticals<br>pharmaceutical adjuvants<br>pharmacodynamics*<br>pharmacogenetics**<br>pharmacokinetics**<br>physiochemical<br>preclinical<br>prediction**<br>prevalidation<br>procedure |
| <b>H</b> | hazard*<br>hazard identification                                                                                                                                                                                                       | <b>R</b> | reduction<br>refinement<br>replacement<br>risk**<br>risk assessment**                                                                                                                                      |
| <b>I</b> | in silico<br>in situ<br>in vitro**<br>in vivo                                                                                                                                                                                          | <b>S</b> | screening test*<br>simulation*<br>slaughterhouse*<br>software**<br>statistics**                                                                                                                            |
|          |                                                                                                                                                                                                                                        | <b>T</b> | teaching**<br>techniques*<br>tests*<br>tiered testing<br>toxicity*<br>toxicity testing*<br>toxicity tests**<br>toxicodynamics<br>toxicokinetics*                                                           |
|          |                                                                                                                                                                                                                                        | <b>V</b> | training*<br>vaccines**<br>validation<br>validation process*                                                                                                                                               |

## Context dependent terms of LOW BREADTH relating to project subjects and specification

(in alphabetical order)

- |                                  |                                                                                                                                                                                                                                                                                                                                                                       |                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>A animal conditions e.g.</b>  | <ul style="list-style-type: none"> <li>distress**</li> <li>eustress</li> <li>harm</li> <li>hormonal control*</li> <li>hormonal regulation*</li> <li>metabolic disorder*</li> <li>pain**</li> <li>stress*</li> <li>stress response*</li> </ul>                                                                                                                         |                            | <ul style="list-style-type: none"> <li>drug resistance**</li> <li>drug synergy*</li> <li>drug therapy**</li> <li>drug toxicity**</li> </ul>                                                                                                                                                                                                                                                                                                                                                                         |
| <b>A animal handling* e.g.</b>   | <ul style="list-style-type: none"> <li>anesthesia**</li> <li>analgesia**</li> <li>behavioural enrichment</li> <li>cage*</li> <li>caging</li> <li>euthanasia**</li> <li>handling**</li> <li>invasive</li> <li>keeping</li> <li>noninvasive</li> <li>parenteral administration*</li> <li>post-surgery</li> <li>post-operative</li> <li>restraint of animals*</li> </ul> | <b>I in vitro** e.g.</b>   | <ul style="list-style-type: none"> <li>animal cell**</li> <li>animal organs*</li> <li>animal tissue**</li> <li>cells**</li> <li>cell culture**</li> <li>cell fractionation**</li> <li>cell line**</li> <li>cellular</li> <li>cell organelle*</li> <li>cytosolic fraction*</li> <li>dermal equivalent</li> <li>embryo culture*</li> <li>explants**</li> <li>membranes**</li> <li>organ culture**</li> <li>subcellular fractions**</li> <li>tissues**</li> <li>tissue culture**</li> <li>tissue equivalent</li> </ul> |
| <b>A animal husbandry** e.g.</b> | <ul style="list-style-type: none"> <li>environmental</li> <li>environmental enrichment**</li> <li>housing</li> <li>husbandry*</li> </ul>                                                                                                                                                                                                                              | <b>M methodology* e.g.</b> | <ul style="list-style-type: none"> <li>artificial intelligence**</li> <li>comparative study**</li> <li>computer simulation**</li> <li>controlled study**</li> <li>EC50</li> <li>ED50</li> <li>e-learning</li> <li>expert systems**</li> <li>inhibitory concentration 50**</li> <li>imaging*</li> <li>LC50</li> <li>lethal dose 50**</li> <li>statistical</li> <li>video recording**</li> <li>virtual reality*</li> </ul>                                                                                            |
| <b>D drugs* e.g.</b>             | <ul style="list-style-type: none"> <li>drug antagonism**</li> <li>drug combinations**</li> <li>drug development**</li> <li>drug discovery</li> <li>drug effects*</li> <li>drug excretion*</li> <li>drug formulations*</li> <li>drug interactions**</li> <li>drug metabolism*</li> <li>drug residues**</li> </ul>                                                      |                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |

### Context dependent terms of LOW BREADTH relating to project subjects and specification

(in alphabetical order)

<b>M</b>	<b>model* e.g.</b>	<ul style="list-style-type: none"> <li>biological model*</li> <li>computer model*</li> <li>disease models*</li> <li>genetic models*</li> <li>mathematical model*</li> <li>prediction model</li> <li>simulation model*</li> <li>theoretical model*</li> <li>transgenic animals*</li> </ul>	<ul style="list-style-type: none"> <li>cytotoxicity*</li> <li>dermal toxicity</li> <li>developmental toxicity**</li> <li>ecotoxicity*</li> <li>embryotoxicity*</li> <li>genotoxicity**</li> <li>immunotoxicity*</li> <li>irritation</li> <li>local toxicity</li> <li>neurotoxicity*</li> <li>organ toxicity</li> <li>phototoxicity**</li> <li>reproductive toxicity*</li> <li>sensitization*</li> <li>subchronic toxicity*</li> <li>systemic toxicity</li> </ul>
<b>T</b>	<b>toxicity*/endpoints* e.g.</b>	<ul style="list-style-type: none"> <li>abnormal toxicity</li> <li>acute toxicity**</li> <li>behavioural toxicity</li> <li>carcinogenicity*</li> <li>chronic toxicity**</li> <li>corrosion*</li> </ul>	

\* terms used as thesaurus terms

\*\* terms used as thesaurus terms with scope notes

**Note:** The preferential listed word variant of terms is the one that mirrors their **predominant usage** within the scientific community. Other variants such singular/plural and BE/AE-language also have to be considered. In the next section Selected Terms with Definition, the corresponding variant of the search terms marked with asterisks is listed.



- This Section is a compilation of relevant THESAURUS 3Rs SEARCH TERMS AND SCOPE NOTES.
- Scope notes define both the MEANING AND CONTEXT OF THESAURUS TERMS.
- USING THESAURUS TERMS IN AN ADVANCED MODE queries (e.g. MeSH-heading-based search) will specifically retrieve documents assigned to the relevant heading (e.g. animal welfare) by an expert review process.
- The thesaurus terms listed here are derived from:
  1. CAB Thesaurus of CAB Abstracts (UK)  
Available from: <http://www.cabi.org/cabthesaurus/>  
Accessed: July 24, 2012
  2. EMTREE Thesaurus of Elsevier B. V. (NL)  
Available from: <http://www.embase.com>  
Accessed: July 24, 2012
  3. MeSH (Medical Subject Headings) Thesaurus of the United States National Library of Medicine (USA)  
Available from: <http://www.nlm.nih.gov/mesh/>  
Accessed: July 24, 2012
  4. NAL Thesaurus of the National Agricultural Library (USA)  
Available from: <http://agclass.nal.usda.gov/>  
Accessed: July 24, 2012

**SELECTED THESAURUS TERMS WITH DEFINITIONS**

*(in alphabetical order)*

TERM	THESAURUS	SCOPE NOTE
<b>acute toxicity</b>	EMTREE	
	NALT	Immediate or short-term adverse reaction of an organism to a single exposure to a chemical substance. (NALT)
<b>anaesthesia</b>	CAB	
<b>analgesia</b>	EMTREE	
	MeSH	Methods of pain relief that may be used with or in place of analgesics. (MeSH)
	NALT	
<b>analysis</b>	CAB	
	EMTREE	
	MeSH	Subheading; Used ... for the identification or quantitative determination of a substance or its constituents and metabolites; includes the analysis of air, water, or other environmental carrier. It excludes the chemical analysis of tissues, tumors, body fluids, organisms, and plants for which “chemistry” is used. The concept applies to both methodology and results. For analysis of substances in blood, cerebrospinal fluid, and urine the specific subheading designating the fluid is used. (MeSH)
<b>anesthesia</b>	EMTREE	
	MeSH	A state characterized by loss of feeling or sensation. This depression of nerve function is usually the result of pharmacologic action and is induced to allow performance of surgery or other painful procedures. (MeSH)
	NALT	
<b>animal</b>	EMTREE	
<b>animal behaviour</b>	CAB	
	NALT	
<b>animal behavior</b>	EMTREE	
<b>animal care</b>	EMTREE	
	NALT	
<b>animal cell</b>	EMTREE	Used for original studies on normal or diseased animal cells. (EMTREE)
<b>animal disease</b>	EMTREE	
<b>animal diseases</b>	CAB	
	MeSH	
	NALT	

TERM	THESAURUS	SCOPE NOTE
<b>animal experiment</b>	EMTREE	Used for original studies using whole animals. (EMTREE)
<b>animal experimentation</b>	MeSH	The use of animals as investigational subjects. (MeSH)
	NALT	Use for the discussion of the use of animals in experiments, typically focused on the effects of experimentation on the behavior or welfare of laboratory animals; Do not use it as a check tag simply denoting the use of laboratory animals in an experiment, for these animals serving in this role USE laboratory animals. (NALT)
<b>animal experiments</b>	CAB	
<b>animal handling</b>	NALT	
<b>animal health</b>	CAB	
	EMTREE	
	NALT	
<b>animal housing</b>	CAB	
	EMTREE	
	NALT	
<b>animal husbandry</b>	CAB	
	EMTREE	
	MeSH	The science of breeding, feeding and care of domestic animals; includes housing and nutrition. (MeSH)
	NALT	
<b>animal model</b>	EMTREE	Used for original studies using animal models of disease (EMTREE)
<b>animal models</b>	CAB	
	NALT	Animals who have specific characteristics that are used in experimental research, teaching or testing in order to study physiology, nutrition, etc. of humans or other species; For animals used to study human disease USE animal disease models; For mathematical models in the study of animal genetics USE mathematical models. (NALT)
<b>animal organs</b>	NALT	
<b>animal production</b>	CAB	
	NALT	
<b>animal rights</b>	EMTREE	
	MeSH	The moral and ethical basis of the protection of animals from cruelty and abuse. The rights are extended to domestic animals, laboratory animals, and wild animals. (MeSH)

TERM	THESAURUS	SCOPE NOTE
<b>animal science</b>	NALT	
<b>animal testing alternative</b>	EMTREE	
<b>animal testing alternatives</b>	CAB	
	MeSH	Procedures, such as Tissue Culture Techniques; mathematical models; etc., when used or advocated for use in place of the use of animals in research or diagnostic laboratories. (MeSH)
<b>animal testing reduction</b>	EMTREE	
<b>animal testing refinement</b>	EMTREE	
<b>animal testing replacement</b>	EMTREE	
<b>animal tissue</b>	EMTREE	Used for original studies on normal or diseased animal tissue. (EMTREE)
<b>animal tissues</b>	NALT	
<b>animal use alternatives</b>	MeSH	Alternatives to the use of animals in research, testing, and education. The alternatives may include reduction in the number of animals used, replacement of animals with a non-animal model or with animals of a species lower phylogenetically, or refinement of methods to minimize pain and distress of animals used. (MeSH)
	NALT	
<b>animal use reduction</b>	NALT	
<b>animal use refinement</b>	NALT	
<b>animal use replacement</b>	NALT	
<b>animal welfare</b>	CAB	
	EMTREE	
	MeSH	The protection of an animal in laboratories or other specific environments by promoting their health through better nutrition, housing, and care. (MeSH)
	NALT	The sum or integration of an animal's past and present states of well-being as it attempts to cope with its environment; and human values concerning the social or ethical aspects of providing that environment. (NALT)
<b>animal wellbeing</b>	EMTREE	
<b>animal well-being</b>	NALT	The current state of an animal living in reasonable harmony with its environment. (NALT)
<b>animals</b>	MeSH	Unicellular or multicellular, heterotrophic organisms, that have sensation and the power of voluntary movement. Under the older five kingdom paradigm, Animalia was one of the kingdoms. Under the modern three domain model, Animalia represents one of the many groups in the domain Eukaryota. (MeSH)

TERM	THESAURUS	SCOPE NOTE
<b>artificial intelligence</b>	EMTREE	
	MeSH	The study and implementation of techniques and methods for designing computer systems to perform functions normally associated with human intelligence, such as understanding language, learning, reasoning, problem solving, etc. (MeSH)
<b>artificial organ</b>	EMTREE	
<b>artificial organs</b>	MeSH	Devices intended to replace non-functioning organs. They may be temporary or permanent. Since they are intended always to function as the natural organs they are replacing, they should be differentiated from prostheses and implants and specific types of prostheses which, though also replacements for body parts, are frequently cosmetic (eye, artificial) as well as functional (artificial, limbs). (MeSH)
<b>assay</b>	EMTREE	
<b>assays</b>	CAB	
	NALT	
<b>autopsy</b>	EMTREE	
	MeSH	Postmortem examination of the body. (MeSH)
<b>bioassay</b>	EMTREE	
<b>biochemistry</b>	CAB	
	EMTREE	
	MeSH	The study of the composition, chemical structures, and chemical reactions of living things. (MeSH)
	NALT	
<b>bioethical issues</b>	MeSH	Clusters of topics that fall within the domain of bioethics, the field of study concerned with value questions that arise in biomedicine and health care delivery. (MeSH)
<b>bioethics</b>	CAB	
	EMTREE	
	MeSH	A branch of applied ethics that studies the value implications of practices and developments in life sciences, medicine, and health care. (MeSH)
	NALT	The study of the ethical and moral implications of new discoveries and practices in the biological sciences, biomedicine, and health care. (NALT)

TERM	THESAURUS	SCOPE NOTE
<b>bioinformatics</b>	CAB	
	EMTREE	
	NALT	A field of biology concerned with the development of techniques for the collection and manipulation of biological data, and the use of such data to make biological discoveries or predictions. This field encompasses all computational methods and theories applicable to molecular biology and areas of computer-based techniques for solving biological problems including manipulation of models and datasets. (NALT)
<b>biological agents</b>	MeSH	Organisms or complex pharmaceutical substances, preparations, or agents of organic origin, usually obtained by biological methods or assay. Biological agents are differentiated from biological factors in that the latter are compounds with biological or physiological activity made by living organisms. (From Webster's 3d ed) (MeSH)
<b>biological markers</b>	MeSH	Measurable and quantifiable biological parameters (e.g., specific enzyme concentration, specific hormone concentration, specific gene phenotype distribution in a population, presence of biological substances) which serve as indices for health- and physiology-related assessments, such as disease risk, psychiatric disorders, environmental exposure and its effects, disease diagnosis, metabolic processes, substance abuse, pregnancy, cell line development, epidemiologic studies, etc. (MeSH)
<b>biological model</b>	EMTREE	
<b>biological product</b>	EMTREE	
<b>biophysics</b>	CAB	
	EMTREE	
	MeSH	The study of physical phenomena and physical processes as applied to living things. (MeSH)
	NALT	
<b>biopsy</b>	CAB	
	EMTREE	
	MeSH	Removal and pathologic examination of specimens in the form of small pieces of tissue from the living body. (MeSH)
	NALT	
<b>cadaver</b>	EMTREE	
	MeSH	A dead body, usually a human body. (MeSH)

TERM	THESAURUS	SCOPE NOTE
<b>cage</b>	EMTREE	
<b>cages</b>	CAB	
	NALT	
<b>capture of animals</b>	CAB	
	NALT	
<b>carcinogenicity</b>	NALT	
<b>case studies</b>	CAB	For medical and veterinary studies use 'case reports'. (CAB)
	NALT	An in-depth examination of a single instance or event. (NALT)
<b>case study</b>	EMTREE	
<b>cells</b>	EMTREE	
<b>cell biology</b>	NALT	
<b>cell culture</b>	CAB	
	EMTREE	
	NALT	A technique for maintaining and/or growing dispersed cells from original tissues, primary culture, cell lines or cell strains. (NALT)
<b>cell fractionation</b>	EMTREE	
	MeSH	Techniques to partition various components of the cell into subcellular fractions. (MeSH)
	NALT	
<b>cell line</b>	EMTREE	
	MeSH	Established cell cultures that have the potential to propagate indefinitely. (MeSH)
<b>cell lines</b>	CAB	
	NALT	
<b>cell organelle</b>	EMTREE	
<b>cells</b>	CAB	
	MeSH	The fundamental, structural, and functional units or subunits of living organisms. They are composed of cytoplasm containing various organelles and a cell membrane boundary. (MeSH)
	NALT	
<b>chemical analysis</b>	CAB	
	EMTREE	
	NALT	
<b>chemical treatment</b>	CAB	
	NALT	
<b>chemicals</b>	CAB	

TERM	THESAURUS	SCOPE NOTE
<b>chemistry</b>	CAB	
	EMTREE	
	MeSH	A basic science concerned with the composition, structure, and properties of matter; and the reactions that occur between substances and the associated energy exchanged. (MeSH)
	NALT	
<b>chronic toxicity</b>	EMTREE	
	NALT	Adverse reaction of an organism to a continuous or repeated exposure to a chemical substance over a long period of time. (NALT)
<b>comparative study</b>	EMTREE	
	MeSH	Publication type; Comparison of outcomes, results, responses, etc for different techniques, therapeutic approaches or other inputs. (MeSH)
<b>computer</b>	EMTREE	
<b>computer model</b>	EMTREE	
<b>computer simulation</b>	CAB	
	EMTREE	
	MeSH	Computer-based representation of physical systems and phenomena such as chemical processes. (MeSH)
<b>computers</b>	CAB	
	MeSH	
	NALT	
<b>controlled study</b>	EMTREE	Used for original studies with a control group, i.e. in which previously defined groups are compared with each other. Also used for studies with control material and control procedures. Retrospective studies may also be included. (EMTREE)
<b>corrosion</b>	CAB	
	MeSH	
<b>cosmetics</b>	CAB	
	NALT	
	MeSH	Substances intended to be applied to the human body for cleansing, beautifying, promoting attractiveness, or altering the appearance without affecting the body's structure or functions. Included in this definition are skin creams, lotions, perfumes, lipsticks, fingernail polishes, eye and facial makeup preparations, permanent waves, hair colors, toothpastes, and deodorants, as well as any material intended for use as a component of a cosmetic product. (U.S. Food & Drug Administration Center for Food Safety & Applied Nutrition Office of Cosmetics Fact Sheet (web page) Feb 1995) (MeSH)

TERM	THESAURUS	SCOPE NOTE
<b>cytosolic fraction</b>	EMTREE	
<b>cytotoxicity</b>	CAB	
	EMTREE	
	NALT	
<b>developmental toxicity</b>	NALT	Adverse effects of toxic substances, including abnormal growth, morphology or physiological function in a developing organism. (NALT)
<b>diagnosis</b>	CAB	
	EMTREE	Used as disease subheading when information is published on the diagnosis of disease or the application of diagnostic tests. (EMTREE)
	MeSH	The determination of the nature of a disease or condition, or the distinguishing of one disease or condition from another. Assessment may be made through physical examination, laboratory tests, or the likes. Computerized programs may be used to enhance the decision-making process. (MeSH)
<b>diagnostic techniques</b>	CAB	
	NALT	
<b>disease model</b>	EMTREE	
<b>disease models</b>	CAB	
	NALT	
<b>disease surveys</b>	CAB	
<b>distress</b>	NALT	An adverse effect on animals when they cannot escape from or adapt to physical or mental stress. (NALT)
<b>drug antagonism</b>	CAB	
	EMTREE	
	MeSH	Phenomena and pharmaceutics of compounds that inhibit the function of agonists (drug agonism) and inverse agonists (drug inverse agonism) for a specific receptor. On their own, antagonists produce no effect by themselves to a receptor, and are said to have neither intrinsic activity nor efficacy. (MeSH)
	NALT	
<b>drug combination</b>	EMTREE	Used as a drug subheading for drugs given in combination or concomitantly. (EMTREE)
<b>drug combinations</b>	MeSH	Single preparations containing two or more active agents, for the purpose of their concurrent administration as a fixed dose mixture. (MeSH)

TERM	THESAURUS	SCOPE NOTE
<b>drug development</b>	CAB	
	EMTREE	Used as a drug subheading for the stages of drug development from screening, isolation and synthesis up to testing in animals, but excluding trials in humans. (EMTREE)
<b>drug effects</b>	CAB	
<b>drug evaluation</b>	MeSH	Any process by which toxicity, metabolism, absorption, elimination, preferred route of administration, safe dosage range, etc., for a drug or group of drugs is determined through clinical assessment in humans or veterinary animals. (MeSH)
	NALT	
<b>drug excretion</b>	CAB	
	EMTREE	
	NALT	
<b>drug formulation</b>	EMTREE	
<b>drug formulations</b>	CAB	
	NALT	
<b>drug interaction</b>	EMTREE	
<b>drug interactions</b>	MeSH	The action of a drug that may affect the activity, metabolism, or toxicity of another drug. (MeSH)
	NALT	
<b>drug metabolism</b>	CAB	
	EMTREE	
<b>drug residue</b>	EMTREE	
<b>drug residues</b>	CAB	
	MeSH	Drugs and their metabolites which are found in the edible tissues and milk of animals after their medication with specific drugs. This term can also apply to drugs found in adipose tissue of humans after drug treatment. (MeSH)
	NALT	
<b>drug resistance</b>	CAB	
	EMTREE	Used as a disease subheading to identify a disease for which resistance to drug treatment (other than drug tolerance) is a significant aspect. (EMTREE)
	MeSH	Diminished or failed response of an organism, disease or tissue to the intended effectiveness of a chemical or drug. It should be differentiated from drug tolerance which is the progressive diminution of the susceptibility of a human or animal to the effects of a drug, as a result of continued administration. (MeSH)
	NALT	
<b>drug screening</b>	EMTREE	

TERM	THESAURUS	SCOPE NOTE
<b>drug synergy</b>	CAB	
<b>drug synergism</b>	MeSH	The action of a drug in promoting or enhancing the effectiveness of another drug. (MeSH)
	NALT	
<b>drug therapy</b>	CAB	
	EMTREE	Used as a drug subheading to identify a drug used to treat disease (including curative, palliative, symptomatic or prophylactic treatment). (EMTREE) Used as a disease subheading to identify a disease or condition treated with a drug. (EMTREE)
	MeSH	
	NALT	
<b>drug toxicity</b>	CAB	
	EMTREE	Used as a drug subheading to identify a drug or chemical that is toxic in animals (including LD50 tests), in animal or human cells and tissues, and in other toxicity studies. In humans, used to signal toxicity at non-therapeutic dose ranges, or when lasting damage is caused at therapeutic dose ranges. (EMTREE)
	MeSH	Manifestations of the adverse effects of drugs administered therapeutically or in the course of diagnostic techniques. It does not include accidental or intentional poisoning for which specific headings are available. (MeSH)
	NALT	
<b>drugs</b>	CAB	
	NALT	Any chemical compounds, including nutrients, that are used in the prevention, diagnosis, treatment, or cure of disease, for the relief of pain, or to control or improve any physiological or pathological disorder in humans or animals. (NALT)
<b>ecotoxicity</b>	EMTREE	
<b>ecotoxicology</b>	EMTREE	
	MeSH	The study of environmental pollution and the toxic effects of environmental pollutants on the ecosystem. The term was coined by Truhaut in 1969. (MeSH)
	NALT	The term was first coined in 1969 by René Truhaut. The science of poisons and toxic substances occurring in the environment and their effects. Can be further expanded as the science of predicting effects of potentially toxic agents on natural ecosystems and nontarget species. (NALT)

TERM	THESAURUS	SCOPE NOTE
<b>education</b>	CAB	
	EMTREE	
	MeSH	Acquisition of knowledge as a result of instruction in a formal course of study. (MeSH)
	NALT	
<b>embryo culture</b>	CAB	
	EMTREE	
	NALT	
<b>embryo culture techniques</b>	MeSH	The technique of maintaining or growing mammalian embryos in vitro. This method offers an opportunity to observe embryonic development; metabolism; and susceptibility to teratogens. (MeSH)
<b>embryotoxicity</b>	EMTREE	
	NALT	
<b>endpoints</b>	NALT	
<b>enrichment</b>	CAB	
<b>environmental enrichment</b>	EMTREE	
	NALT	Modification of the physical environment of animals, especially those in captivity, for the purpose of meeting behavioral needs and improving well-being. (NALT)
<b>ethics</b>	CAB	
	EMTREE	
	MeSH	The philosophy or code pertaining to what is ideal in human character and conduct. Also, the field of study dealing with the principles of morality. (MeSH)
	NALT	
<b>euthanasia</b>	CAB	
	EMTREE	
	MeSH	The act or practice of killing or allowing death from natural causes, for reasons of mercy, i.e., in order to release a person from incurable disease, intolerable suffering, or undignified death. (from Beauchamp and Walters, Contemporary Issues in Bioethics, 5th ed) (MeSH)
	NALT	
<b>evaluation</b>	CAB	
	EMTREE	
<b>ex vivo study</b>	EMTREE	
<b>experimental animal</b>	EMTREE	

TERM	THESAURUS	SCOPE NOTE
<b>experimental animal welfare</b>	EMTREE	
<b>experimental design</b>	CAB	
	EMTREE	
	NALT	
<b>expert system</b>	EMTREE	
<b>expert systems</b>	CAB	
	MeSH	Computer programs based on knowledge developed from consultation with experts on a problem, and the processing and/or formalizing of this knowledge using these programs in such a manner that the problems may be solved. (MeSH)
	NALT	
<b>explant</b>	EMTREE	
<b>explants</b>	CAB	
	NALT	Parts of a living organism, such as cells, tissues, or organs, which are transferred to an artificial medium for culture. (NALT)
<b>food hygiene</b>	CAB	
<b>genetic model</b>	EMTREE	
<b>genetic models</b>	CAB	
<b>genetics</b>	CAB	
	EMTREE	
	MeSH	The branch of science concerned with the means and consequences of transmission and generation of the components of biological inheritance. (Stedman, 26th ed) (MeSH)
	NALT	
<b>genotoxicity</b>	CAB	
	EMTREE	
	NALT	The degree to which a toxin has adverse effects on DNA. (NALT)
<b>handling</b>	CAB	
	MeSH	Physical manipulation of animals and humans to induce a behavioral or other psychological reaction. In experimental psychology, the animal is handled to induce a stress situation or to study the effects of "gentling" or "mothering". (MeSH)
<b>hazard</b>	EMTREE	
<b>hazards</b>	CAB	
<b>hormonal control</b>	CAB	
<b>hormonal regulation</b>	EMTREE	

TERM	THESAURUS	SCOPE NOTE
	NALT	
<b>housing</b>	NALT	Use only for housing for humans; For housing for animals USE animal housing. (NALT)
<b>humane endpoints</b>	NALT	An early endpoint that, while accomplishing the research objectives, is chosen to minimize or terminate the pain or distress of the experimental animals rather than waiting for their deaths as the endpoint. (NALT)
<b>husbandry</b>	CAB	
<b>imaging</b>	EMTREE	
<b>immunology</b>	CAB	
	EMTREE	
	NALT	
<b>immunotoxicity</b>	EMTREE	
	NALT	
<b>in vitro</b>	CAB	
	MeSH	Publication type; Studies using excised tissues. (MeSH)
<b>in vitro study</b>	EMTREE	
<b>in vitro studies</b>	NALT	
<b>inhibitory concentration 50</b>	MeSH/NALT	The concentration of a compound needed to reduce population growth of organisms, including eukaryotic cells, by 50% in vitro. Though often expressed to denote in vitro antibacterial activity, it is also used as a benchmark for cytotoxicity to eukaryotic cells in culture. (MeSH, NALT)
<b>laboratory animal science</b>	MeSH	The science and technology dealing with the procurement, breeding, care, health, and selection of animals used in biomedical research and testing. (MeSH)
<b>laboratory animals</b>	CAB	
	MeSH	
	NALT	Experimental animals used either as the subject of research or as an experimental tool; For animal models of human diseases USE animal models; For mathematical models, e.g. animal genetics, USE mathematical models. (NALT)
<b>lethal dose 50</b>	MeSH	The dose amount of poisonous or toxic substance or dose of ionizing radiation required to kill 50% of the tested population. (MeSH)
	NALT	The amount of a single dose of a solid or liquid substance required to kill 50% of the tested population. It is usually expressed in mg/kg (mg of material per kilogram of body weight) and is used for all routes of exposure other than inhalation. Compare "lethal concentration 50". (NALT)

TERM	THESAURUS	SCOPE NOTE
<b>licensing</b>	EMTREE	
<b>licensure</b>	MeSH	The legal authority or formal permission from authorities to carry on certain activities which by law or regulation require such permission. It may be applied to licensure of institutions as well as individuals. (MeSH)
<b>mathematical model</b>	EMTREE	
<b>mathematical models</b>	CAB	
	NALT	
<b>membrane</b>	EMTREE	
<b>membranes</b>	CAB	
	MeSH	Thin layers of tissue which cover parts of the body, separate adjacent cavities, or connect adjacent structures. (MeSH)
<b>metabolic disorder</b>	EMTREE	
<b>metabolism</b>	CAB	
	EMTREE	
	MeSH	The chemical reactions that occur within the cells, tissues, or an organism. These processes include both the biosynthesis (anabolism) and the breakdown (catabolism) of organic materials utilized by the living organism. (MeSH)
	NALT	
<b>methodology</b>	CAB	
	EMTREE	
	NALT	
<b>methods</b>	MeSH	
<b>microbiology</b>	CAB	
	EMTREE	
	MeSH	The study of microorganisms such as fungi, bacteria, algae, archaea, and viruses. (MeSH)
	NALT	
<b>model</b>	EMTREE	
<b>models</b>	CAB	
	NALT	
<b>molecular biology</b>	CAB	
	EMTREE	
	MeSH	A discipline concerned with studying biological phenomena in terms of the chemical and physical interactions of molecules. (MeSH)
	NALT	
<b>natural products</b>	CAB	

TERM	THESAURUS	SCOPE NOTE
<b>neurobiology</b>	EMTREE	
	MeSH	The study of the structure, growth, activities, and functions of neurons and the nervous system. (MeSH)
<b>neurology</b>	CAB	
	EMTREE	
	MeSH	A medical speciality concerned with the study of the structures, functions, and diseases of the nervous system. (MeSH)
<b>neurotoxicity</b>	CAB	
	EMTREE	
	NALT	
<b>nutrition</b>	CAB	
	EMTREE	
	NALT	
<b>nutritional sciences</b>	MeSH	The study of nutrition processes as well as the components of food, their actions, interaction, and balance in relation to health and disease. (MeSH)
<b>oncology</b>	EMTREE	
<b>organ</b>	EMTREE	
<b>organ culture</b>	CAB	
	EMTREE	
	NALT	Maintenance or growth of animal organs in vitro, originating from three-dimensional cultures of undissociated cells in a manner that retains some or all of the histological features of the tissue in vivo. (NALT)
<b>organ culture techniques</b>	MeSH	A technique for maintenance or growth of animal organs in vitro. It refers to three-dimensional cultures of undissociated tissue retaining some or all of the histological features of the tissue in vivo. (Freshney, Culture of Animal Cells, 3d ed, p1) (MeSH)
<b>organelles</b>	CAB	
	MeSH	Specific particles of membrane-bound organized living substances present in eukaryotic cells, such as the mitochondria; the golgi apparatus; endoplasmic reticulum; lysosomes; plastids; and vacuoles. (MeSH)
	NALT	
<b>organs</b>	CAB	
<b>pain</b>	CAB	
	EMTREE	
	MeSH	An unpleasant sensation induced by noxious stimuli which are detected by nerve endings of nociceptive neurons. (MeSH)

TERM	THESAURUS	SCOPE NOTE
	NALT	
<b>parasitology</b>	CAB	
	EMTREE	
	MeSH	The study of the structure, growth, function, genetics and reproduction of parasites and parasitic diseases. (MeSH)
	NALT	
<b>parenteral administration</b>	CAB	
<b>pathogens</b>	CAB	
	NALT	Microorganisms, viruses and parasites that can cause disease. (NALT)
<b>pharmacodynamics</b>	CAB	
	EMTREE	
<b>pharmacogenetics</b>	EMTREE	
	MeSH	A branch of genetics which deals with the genetic variability in individual responses to drugs and drug metabolism (biotransformation). (MeSH)
<b>pharmacokinetics</b>	CAB	
	EMTREE	Used as a drug subheading for the kinetics of absorption, distribution, biotransformation or elimination of a drug in humans and animals. (EMTREE)
	MeSH/ NALT	Dynamic and kinetic mechanisms of exogenous chemical and drug absorption, biological transport, tissue distribution, biotransformation; elimination; and toxicology as a function of dosage, and rate of metabolism. It includes toxicokinetics, the pharmacokinetic mechanism of the toxic effects of a substance. ADME and ADMET are short-hand abbreviations for absorption, distribution, metabolism, elimination and toxicology. (MeSH, NALT)
<b>pharmacology</b>	CAB	
	EMTREE	Used as a drug subheading for the mechanism of action of a drug, including drug binding to receptors and drug sensitivity/resistance studies (other than for microorganisms). (EMTREE)
	MeSH	The study of the origin, nature, properties, and actions of drugs and their effects on living organisms. (MeSH)
	NALT	
<b>pharmacy</b>	CAB	
	EMTREE	
	MeSH	The practice of compounding and dispensing medicinal preparations. (MeSH)
<b>phototoxicity</b>	CAB	
	NALT	The adverse condition due to overexposure to light. (NALT)

TERM	THESAURUS	SCOPE NOTE
<b>physiology</b>	CAB	
	EMTREE	
	MeSH	The biological science concerned with the life-supporting properties, functions and processes of living organisms or their parts. (MeSH)
	NALT	
<b>prediction</b>	CAB	
	EMTREE	
	NALT	The prediction or projection of the nature of future problems or existing conditions based upon the extrapolation or interpretation of existing scientific data or by the application of scientific methodology. (NALT)
	NALT	
<b>reproductive toxicology</b>	NALT	Study of the adverse effects of substances on the embryo, fetus, neonate and prepubertal mammal and the adult reproductive and neuroendocrine systems. (NALT)
<b>restraint of animals</b>	CAB	
	NALT	
<b>risk</b>	CAB	
	EMTREE	
	MeSH	The probability that an event will occur. It encompasses a variety of measures of the probability of a generally unfavorable outcome. (MeSH)
	NALT	
<b>risk assessment</b>	CAB	The evaluation of the likelihood of a particular risk happening and/or the consequences if it does happen. (CAB)
	EMTREE	
	MeSH	The qualitative or quantitative estimation of the likelihood of adverse effects that may result from exposure to specified health hazards or from the absence of beneficial influences. (Last, Dictionary of Epidemiology, 1988) (MeSH).
	NALT	The qualitative or quantitative evaluation of the likelihood of adverse effects. A risk assessment generally has four steps: hazard identification, hazard characterization, exposure assessment and risk characterization. (NALT)
<b>screening</b>	CAB	Systematic examination of subjects to determine presence or absence or degree of some characteristic. (CAB)
	NALT	A systematic examination or assessment, done to detect a particular substance or attribute. (NALT)
<b>screening test</b>	EMTREE	

TERM	THESAURUS	SCOPE NOTE
<b>sensitization</b>	EMTREE	
<b>simulation</b>	EMTREE	
<b>simulation models</b>	CAB	
	CAB	
<b>slaughterhouse</b>	NALT	
	EMTREE	
<b>slaughterhouses</b>	NALT	
<b>software</b>	MeSH	Sequential operating instructions for a particular problem or function to be run on a digital computer. (MeSH)
<b>statistics</b>	CAB	
	EMTREE	
	MeSH	Publication type; Works consisting of presentations of numerical data on particular subjects. (MeSH)
	NALT	
<b>stress</b>	CAB	Physiological. (CAB)
	EMTREE	
<b>stress response</b>	CAB	
<b>subcellular fractions</b>	MeSH/ NALT	Components of a cell produced by various separation techniques which, though they disrupt the delicate anatomy of a cell, preserve the structure and physiology of its functioning constituents for biochemical and ultrastructural analysis. (From Alberts et al., Molecular Biology of the Cell, 2d ed, p163) (MeSH, NALT)
<b>subchronic toxicity</b>	NALT	
<b>teaching</b>	CAB	
	EMTREE	
	MeSH	The educational process of instructing. (MeSH)
<b>techniques</b>	CAB	
<b>tests</b>	CAB	
<b>theoretical model</b>	EMTREE	
<b>tissue</b>	EMTREE	
<b>tissue culture</b>	CAB	
	EMTREE	
	NALT	A method of maintaining or growing tissues, organ primordia, whole or parts of organs, in a manner to preserve their structures and/or function. (NALT)
<b>tissue cultures</b>	CAB	Properties of cultures; for culture techniques use 'tissue culture'. (CAB)
<b>tissue culture techniques</b>	MeSH	A technique for maintaining or growing tissue in vitro, usually by diffusion, perfusion, or perfusion. The tissue is cultured directly after removal from the host without being dispersed for cell culture. (MeSH)

TERM	THESAURUS	SCOPE NOTE
<b>tissues</b>	CAB	
	MeSH	Collections of differentiated cells, such as epithelium; connective tissue; muscles; and nerve tissue. Tissues are cooperatively arranged to form organs with specialized functions such as respiration; digestion; reproduction; movement; and others. (MeSH)
<b>toxicity</b>	CAB	
	EMTREE	
	NALT	
<b>toxicity testing</b>	EMTREE	
	NALT	
<b>toxicity tests</b>	MeSH	An array of tests used to determine the toxicity of a substance to living systems. These include tests on clinical drugs, foods, and environmental pollutants. (MeSH)
<b>toxicokinetics</b>	EMTREE	
<b>toxicology</b>	CAB	
	EMTREE	
	MeSH	The science concerned with the detection, chemical composition, and biological action of toxic substances or poisons and the treatment and prevention of toxic manifestations. (MeSH)
	NALT	
<b>training</b>	CAB	
	EMTREE	
<b>transgenic animal</b>	EMTREE	
<b>transgenic animals</b>	CAB	
	NALT	
<b>vaccine</b>	EMTREE	
<b>vaccines</b>	CAB	
	MeSH	Suspensions of killed or attenuated microorganisms (bacteria, viruses, fungi, protozoa, or rickettsiae), antigenic proteins derived from them, or synthetic constructs, administered for the prevention, amelioration, or treatment of infectious and other diseases. (MeSH)
	NALT	
<b>validation process</b>	EMTREE	
<b>video recording</b>	MeSH	The storing or preserving of video signals for television to be played back later via a transmitter or receiver. Recordings may be made on magnetic tape or discs (videodisc recording). (MeSH)
<b>videorecording</b>	EMTREE	
<b>virtual reality</b>	EMTREE	



# 3Rs SEARCH PROCEDURE

## the seven golden steps and checklist

- This section provides a generic INFORMATION SEARCH PROCEDURE COMPOSED OF SEVEN STEPS. The search procedure is optimised to retrieve information relating to the 3Rs, yet remain flexible enough to be adapted for other purposes.
- All successful search procedures for animal use alternatives start by DEFINING THE INFORMATION NEEDS. Only then can the most appropriate INFORMATION RESOURCES BE SELECTED, and relevant SEARCH TERMS COMPILED.
- Systematic searches should begin using a 3Rs-SPECIFIC RESOURCE such as DB-ALM of EURL ECVAM (EC-JRC, IHCP) or AnimAlt-ZEBET of the BfR (Germany).
- Thereafter, if necessary the “SEARCH HORIZON” can be gradually BROADENED by using broader coverage databases.

#### **THE SEVEN GOLDEN STEPS TO SUCCESSFUL SEARCHING**

**Step 1: Clearly Define and Be Aware of Your Specific Information Need**

**Step 2: Identify the Fundamental Components of Your Scientific Approach**

**Step 3: Choose the Most Appropriate Information Resources**

**Step 4: Compile Essential and Relevant Search Terms**

**Step 5: Start Your Search with a Simple Query in a 3Rs Specific Context**

**Step 6: Selectively Limit Search Results from More Extensive Resources**

**Step 7: Broaden the Search Horizon**

**STEP 1:****CLEARLY DEFINE AND BE AWARE OF YOUR SPECIFIC INFORMATION NEED****Level of Knowledge and the State of the Art**

An essential part of the planning of any research or testing programme is gathering and reviewing available information about the current level of **knowledge about the specific research objective, potential research strategies and methods** – with a view to identifying and making appropriate use of appropriate methods to replace, reduce or refine proposed animal use.

Unless and until this has been done, documentation cannot be prepared for evaluation for funding, local ethical approval, or national regulatory approval.

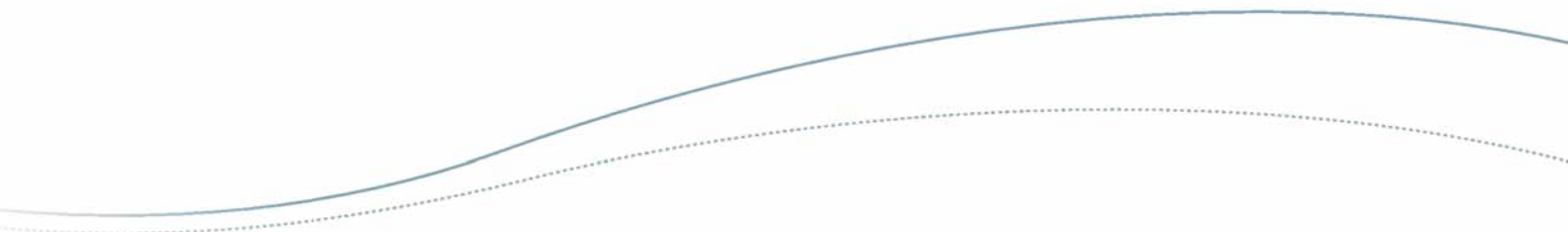
**Indispensability**

When a research proposal involving the use of animals requires regulatory approval, the onus is on the applicant to exercise due diligence with respect to demonstrating that all reasonable efforts have been made to find and take account of 3Rs opportunities.

The key aims of information searches undertaken at the planning stage is to both determine the **availability and suitability of alternatives**, and provide evidence to make the case that the proposed animal use is the most humane way of meeting the scientific objectives.

**An animal experiment to achieve any defined scientific objective cannot be deemed to be indispensable unless and until the non-availability of suitable alternatives is established.**

**Scientists have to supply information on the non-availability of alternative methods according to the 3Rs principle** (see Annex I - Legal Background for Information Requirements). In addition they may have to justify why some seemingly relevant alternatives are not suitable.



**STEP 2:****IDENTIFY THE FUNDAMENTAL COMPONENTS OF YOUR SCIENTIFIC APPROACH****Any search for specific information starts with a sheet of paper!**

Before using the computer to access search engines or database hosts, the **specific scientific objectives being pursued, and the potential strategies and methods of achieving these objectives need to be clearly defined.** (65) This is part of the prospective planning of your search.

Only then can consideration be given to the most appropriate information resources; and the most powerful search terms; and potential limitations of the findings of the initial information searches.

**Field of Investigation**

The specific field of investigation (e.g. animal health, risk assessment, education, or gene function studies) is relevant to the **choice of preferred information sources.** Individual sources generally focus on certain fields and are weak in others.

Therefore, begin by considering the coverage of different sources in relation to your information need:

- If a planned **animal use is required by official regulations**, e.g. Council Regulation (EC) No 440/2008 (REACH) (66), in many cases suitable alternative methods will need to comply with specific regulatory guidelines. In this context the best potential information sources include added-value resources like “DB-ALM” and “AnimAlt-ZEBET” or relevant web sites like “AltTOX.org”.
- Information on **animal use alternatives for educational purposes** will generally be best retrieved from specialised databases, such as “NORINA” or web sites like the “eurca”.
- Scientists involved in **basic research** should begin by placing reliance in high quality peer reviewed sources: these should provide access to the literature relevant to scientifically accepted techniques that have withstood peer review.

The resources listed above and elsewhere in the EURL ECVAM Search Guide for original scientific information (see Volume “Data Sheets-Information Resources” of the EURL ECVAM Search Guide) were evaluated by checking their indexing in high-ranking scientific database “institutions” like MEDLINE.

You should also consider using other added-value resources, such as AnimALT-ZEBET, than can provide structured summaries of alternative methods in basic research.

To support scientists to find and evaluate relevant 3Rs information Section the volume on Information Resources offers structured summaries of the most important features of key information resources for different classes of animal use.

**Objectives**

Relevant search terms cannot be selected until the specific objectives of a research project are clearly defined. Focusing at this stage on the scientific objectives rather than the preferred animal model, allows for search queries that will also elicit **information on different methodical approaches**, particularly replacement options, potentially **relevant to the defined scientific objective** but not previously known to the enquirer.

It may also unearth original scientific findings, sufficiently closely related to the planned animal use, to make the additional studies unnecessary.

### Methods and Models

A specification of the strategy, study design and the models used also helps in deducing relevant search terms.

In contrast to scientific objective-derived search terms, **method-derived terms** are particularly relevant retrieving documents that report **variations and derivations of a given methodical approach**. As a result the documents found are likely to be a particularly good source of reduction and refinement options.

In a 3Rs specific search environment however, method-derived search terms can also be used to target replacement methods developed to substitute for the relevant animal methods.

### Objectives v. Methods

A consideration of whether to initially opt for **objective - or methodology-derived search terms** is also influenced by the properties of the relevant information resources (see next steps).

Except for added-value and full text databases, most databases only allow for **searching the title and the abstract of documents** and other bibliographic information - and not for access to the full text of the articles.

However, in original scientific publications full methodical details are described in the “material and methods” section of the full text documents. Precise methodical details can therefore only be captured by **searching the full text of the publication**. Thus, using methodology-derived terms in “abstract-only” resources is likely to miss a great deal of relevant information.

Abstracts however often clearly describe the author’s research objectives. Therefore, objective based queries can be expected to retrieve a large proportion of relevant documents from “abstract-only” databases. However, the longer hit lists this type of search provides (which will also inevitably contain information that is not relevant) make it time consuming to use such lists for supplementary full text searches looking for relevant methodological details.

### STEP 3: CHOOSE THE MOST APPROPRIATE INFORMATION RESOURCES

As indicated before, **the choice of information sources follows the information needs being defined.**

Appropriate added-value resources should always be the first choice: these list information evaluated by experts in a systematic fashion, making it easier to retrieve the documents most suited to your needs.

The Section Information Resources – General Considerations of this Volume introduces 3Rs-relevant information resources categorised according to the quality and type of information they contain. The Information Resource Inventories (see volume Data Sheets-Information Resources) provide clearly presented overviews to assist in choosing the best information resources for particular information needs.

To support scientists find and evaluate relevant 3Rs information **the volume on Information Resources of the EURL ECVAM Search Guide offers structured summaries of the most important features of key information resources** for different classes of animal use.

### STEP 4 COMPILE RELEVANT AND NECESSARY SEARCH TERMS

Search terms are chosen according to their relevance and specificity. Ideally relevant terms must also be **unique identifiers of the basic components of your scientific approach** (see Step 2) **to discriminate** it from similar but **non-relevant approaches**.

You need consider when and whether to employ **combinations of search terms**, predetermined by context (with information resource):

- If you have chosen a 3Rs specific resource, further addition of “3Rs-topic-defining-terminology” (see Section Search Terms and their Use) to context-dependent terms is unnecessary as the context of your search is already assumed by the resource.
- If you prefer resources, like MEDLINE database, that cover a wide variety of the biomedical literature you will have to limit your search to that subset of documents categorised as relevant to the 3Rs by expert review (see Section Basic Search Principles, advanced search). Thereafter, the deployment of additional “3Rs-topic-defining-terminology” is unnecessary.
- In “broad-coverage” environments which do not have an established 3Rs category, context-dependent terms must be combined with 3Rs-topic-definers.
- In some circumstances combinations of context-dependent terms only may be tried in an attempt to target potentially relevant information that stems work not otherwise associated with the 3Rs. With this method there is no certainty that relevant material will be found – but you can be sure that much which is irrelevant will be found.

Advice on proven “3Rs-topic-defining-terms” and “context-dependent terms” are given in Section Search Terms and their Use.

**STEP 5****START YOUR SEARCH WITH A SIMPLE QUERY IN A 3Rs SPECIFIC CONTEXT**

The frustration caused by poorly conducted information search is generally self-inflicted, and can be prevented in future by following the principles and practice set out in this Guide.

Common causes of unsuccessful information searches include:

- the lack of a awareness of the information need in the absence of a goal-oriented strategy,
- a failure to take account of scientific objectives, methods and context, and
- a tendency to start, and sometimes stop, information searches with intuitive “shots in the dark”.

Efficient and effective searches follow a systematic and structured routine; they capitalise on efforts that have already made to structure information and add expert input. These efforts create “**islands**” of **well-defined and structured information within an “ocean” of inhomogeneous raw information** illustrated in Figure 3 and a sound searching strategy targets these resources.

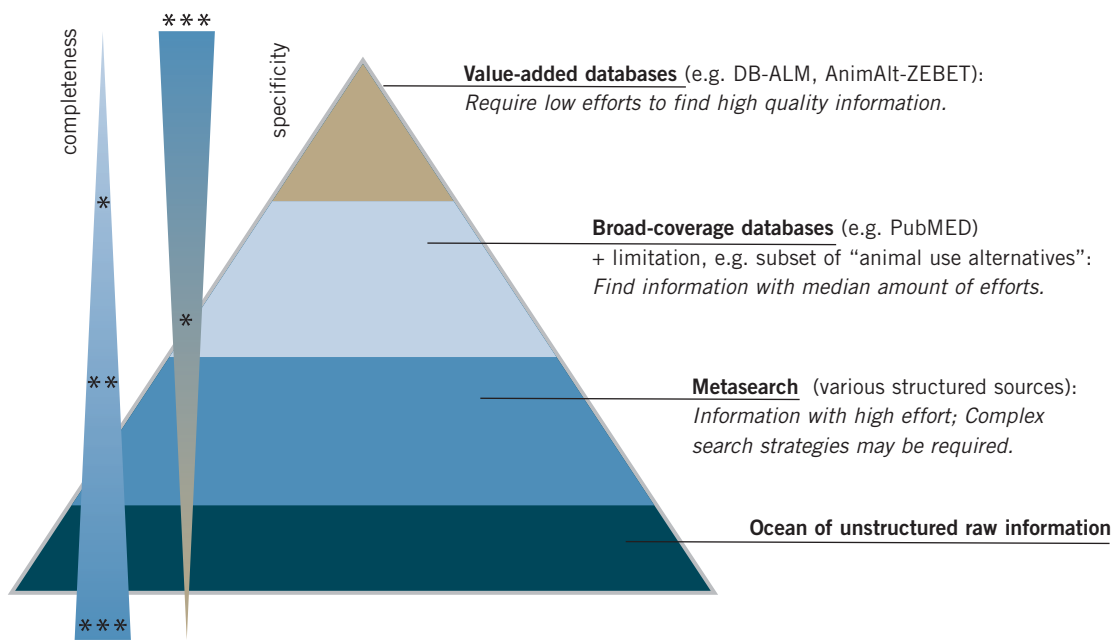


Figure 3: Quality levels of information

The top of the “3Rs-island” is represented by the information that has already been collected, expertly evaluated and ranked about alternative methods. These are the **added-value databases**, such as DB-ALM and AnimAlt-ZEBET. This degree of added value is an essential step in transforming into “knowledge” and insights.

The middle level comprises the information typically found in **broad-coverage databases** such as MEDLINE: again value has been added by structuring the information, linking relevant documents to a 3Rs topic by an indexer or expert review, but without the contexts of the documents having been further evaluated or ranked.

The **lowest level information** stored in structured resources like databases, but has not been categorised in relation to its relevance to the 3Rs, nor has it been expertly evaluated. To obtain specific information you therefore need complex search strategies.

Then, surrounding the structured information island, you find the “ocean”, **websites** accessible via the World-Wide-Web: seemingly limitless amounts of unprocessed information of variable quality and often uncertain provenance.

As you move from top to bottom information quality decreases, and volume of information increases making it difficult to find the information you need.

As your objective is to efficiently and effectively retrieve quality customized information about relevant alternative methods, your **starting point will typically be a value-added 3Rs specific database**. The number of available documents in these databases is easy to handle (sometimes < 1,000), the context is already assumed and some expert review has already taken place, and the resulting searching strategy and selection of search terms is relatively straightforward. Sometimes all that may be necessary to obtain all you need is simply trying out several search terms, or even just browsing through the inventory. In some cases your information needs may be satisfied at this point.

## STEP 6:

### LIMIT SEARCH RESULTS FROM MORE EXTENSIVE RESOURCES

In the event that added-value databases are not suited to your needs, then you should use a **lower ranking, broader coverage, biomedical database**.

Always choose one that allows you to use appropriate search terms and tools to limit the pool of searchable documents to the subset relevant to the 3Rs. This is best achieved by selecting resources where documents have been pre-assigned to a 3Rs-relevant heading, e.g. *animal use alternatives*, during a formal indexing process.

Even so, the number of documents (relevant and irrelevant) identified by preliminary searches will tend to be high. Before seeking to reduce this number by entering additional search terms, consider using the commonly available option of specifying the number of documents you wish to see at any one time, and asking that only title and abstract are shown.

Then, if necessary, **refine your search query**. Consider using supplementary:

- methodology-derived terms to focus on variations and derivations of given methodical approach
- objective-derived search terms to capture more documents relating your desired scientific outcomes (see before)

Also consider the possible word morphologies and synonyms of the terms and use the given tools (e.g. wildcards) to capture relevant variations (refer to Section Basic Search Principles for details).

Apply these methods to optimise your query to limit the number of retrieved documents within a maximum pre-determined number of relevant documents.

The product is a list of documents derived from your search terms and strategy. Most search engines provide options to **arrange this list** in different ways. In PubMed for example, you can sort documents according to publication date, journal, author name or title.

At this stage the content of the retrieved and sorted **documents has to be evaluated** by scanning the title, the abstract and the assigned keywords (i.e. chose the “citation” display in PubMed to uncover the “MeSH-terms” assigned to a document). Remember the main limitations of “abstract-only” documents outlined in Step 1, and remember that when the information source has been working with full text documents that the material and methods section may be of special interest.

## STEP 7: BROADEN THE SEARCH HORIZON

### Too little information?

If you get this far, but have found little or no relevant information for your specific information you need then stop and think about possible deficiencies in your search. Some of the commoner problems include:

- selecting search terms which are too specific, or having chosen the most unusual synonyms
- inappropriate usage of Boolean operators, context operators or parenthesis
- being too prescriptive about search limitations (e.g. publication year, publication type etc.)

The most relevant documents of the first list may render some clues for an improved search terminology. Having reflected on the reasons for too little (just as in the case of retrieving too much) information, you will be in a good position to **conduct a supplementary search**.

Techniques to improve the completeness of a search include broadening **the search horizon by using larger sources of information**, and lessening the restrictions on the information to be excluded from the search. Repeat Step 6 in the broad coverage resources with fewer limitations. You might then proceed to resources with even broader coverage (e.g. meta-databases).

You may ultimately end up combining previously successful search terms using either a more general database or an all-purpose internet search engine: make sure you also find a way of specifying the appropriate context. Also consider limiting the documents as described, or make use of innovative **semantic search tools** like “Go3R” (see Section Web Search Engines in the volume on Information Resources).



- The 3Rs search procedure checklist is designed to:
  - **PUT INTO PRACTICE THE PRINCIPLES** set out elsewhere in the ECVAM Search Guide as “**THE SEVEN GOLDEN STEPS TO SUCCESSFUL SEARCHING**”,
  - obtain information of the quality required to both consider relevant alternatives, and justify any necessary animal use.
- Using the 3Rs search procedure checklist enables scientists to construct **SYSTEMATIC AND EFFICIENT SEARCHES**.
- It includes items that are specific for searching information on alternative methods.

**STEP 1. INFORMATION NEED**

- Clearly define your specific information need:

**STEP 2. COMPONENTS OF YOUR APPROACH**

- Identify the fundamental components of your scientific approach.
- Field of investigation:
  - Specific objective(s):
  - Methods/Models:

**STEP 3. APPROPRIATE INFORMATION RESOURCES**

- Define the most appropriate information resources.
- Value-added:
  - Limitable (to a 3Rs-subset of documents) broad coverage: indicate what limitations you plan to use (e.g. MeSH-term-based: *animal use alternatives*).
  - Unlimited broad coverage.

**STEP 4. RELEVANT SEARCH TERMS**

- Compile the search terms that best describe your scientific objectives and approach, and need for 3Rs information.  
Select terms with appropriate levels of specificity/breadth.  
Consider thesaurus terms, and advanced queries.
- Field of investigation:
  - Objectives:
  - Methods/Models:

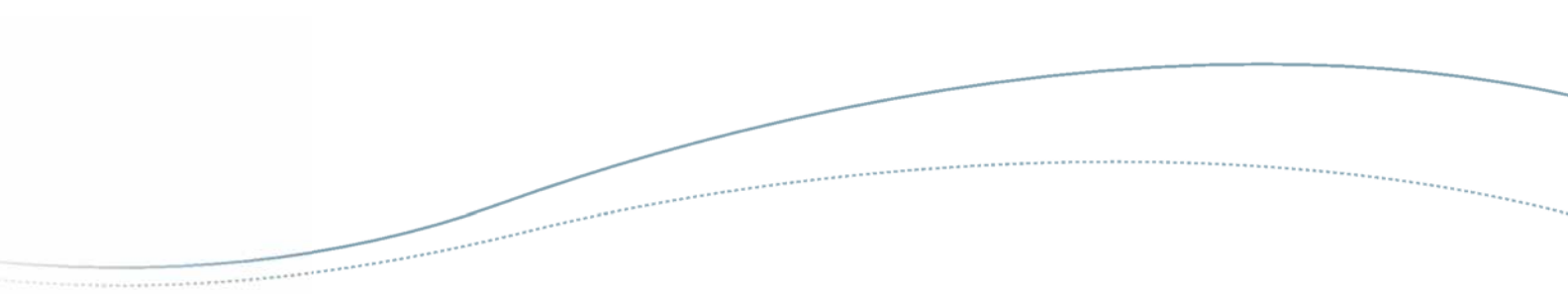
**STEP 5 START YOUR SEARCH WITH A SIMPLE QUERY IN A 3Rs SPECIFIC CONTEXT**

- Start your search in value-added 3Rs sources, trying out different search terms within a simple query, and browsing through the inventory (classification scheme) if available.
- Evaluate the documents retrieved.  
Is there information on alternative method(s) that are suitable to reach the scientific purpose of your approach, are there potentially better search terms?

**STEP 6 LIMIT SEARCH RESULTS FROM MORE EXTENSIVE RESOURCES**

- If no information on suitable alternatives is found using the value-added sources, continue your search using limitable broad coverage sources.
- Try different kinds of 3Rs-relevant limitations (e.g. MeSH-term-based, journal-based etc) to limit the results to relevant and manageable lists of documents. Evaluate the results and consider if it is possible to improve your query by adding varying search terms and Boolean operators.
- Evaluate the most relevant documents retrieved.

**STEP 7 BROADEN THE SEARCH HORIZON**

- If no suitable alternative was retrieved by restricting the search by predetermined 3Rs-relevant limitations, repeat step 5 in broader coverage resources with more general limitations consistent with your scientific methodology and objectives.
  - Evaluate the documents retrieved.
- 

## CHECK LIST EXAMPLES

### 3Rs Search Procedures

This Section provides **working examples** following  
“The Seven Golden Steps to Successful Searching” for:

- **Eye Corrosion**
- **Potency Testing of Botulinum Toxin**

## EYE CORROSION

### Background

The European REACH regulation (1907/2006/EC) requires that all substances manufactured in the EU, or imported into the EU, in quantities in excess of 1 tonne are assessed for health and safety and environmental purposes. As the REACH provisions are phased in the initially assessed materials are “substances of very high concern” to the human health or the environment. Safety evaluations are also required for plant protection (91/414/EEC) and biocidal products (98/8/EC) and for cosmetics (76/768/EEC).

The European Council Regulation No 440/2008 (the “Test Methods Regulation”), and OECD guidelines, specify how the potential harm inflicted by a chemical must be characterised. OECD Test Guideline (TG 405) specifies how the “**acute eye irritation/corrosion**” potential of a chemical has to be characterised: **the rabbit Draize eye test** is the reference test method for determining the potential of chemicals to cause damage to the eye.

OECD TG 405 also makes provision for an integrated testing strategy (ITS) using a weight-of-evidence (WoE) approach for the evaluation of existing data on the eye irritation/corrosion properties of substances, and a tiered approach for the generation of additional relevant data on substances for which additional data are needed. In this tiered approach scientifically **validated *in vitro* and *ex vivo* methods** must be used if appropriate before the rabbit test according to TG 405 is conducted as a last resort.

As *in vitro* test methods are accepted for pre-validation and are validated, it is anticipated the range of test materials that will require *in vivo* testing will steadily reduce – and testing practices will have to be adjusted accordingly.

### Scenario

Consider the case of **a company within the EU is producing 5 tonnes of a chemical per annum (tpa)**.

To comply with the REACH regulation, the company has to predict or demonstrate the **potential of the chemical to cause ocular damage**: existing test data will have to be reviewed, and if appropriate additional *in vitro* or *in vivo* testing commissioned.

The REACH “Endpoint Specific Guidance” requires that the testing data regarding the corrosivity has to be derived only from *in vitro* methods when the substance quantity is below 10 tpa.

Thus, the company needs to know about the current validation status of alternative method(s) to substitute for the Draize eye test, and/or the most refined *in vivo* protocol used for regulatory purposes.

**STEP 1. INFORMATION NEED**

- Clearly define your specific information need:  
**To find validated in vitro methods, and the more refined in vivo methods, to determine the ocular safety of a specific chemical to satisfy the REACH requirements (within the EU).**

*NOTE* Please refer to The Seven Golden Steps for creating a 3Rs Search Procedure (page 80) for a discussion of various needs for information retrieval during the planning and the application of a project that involves the use of animals.

**STEP 2. COMPONENTS OF YOUR APPROACH**

- Identify the fundamental components of your scientific approach.
- a. Field of investigation:  
**toxicology; toxicity testing**
  - b. Specific objective(s):  
**to determine the ocular irritancy potential of a specific chemical**
  - c. Methods/Models:  
**Draize test, rabbit eye**

*NOTE* In this case, it is quite simple to draft the objective, because it is predetermined by the official regulations (REACH).

**STEP 3. APPROPRIATE INFORMATION RESOURCES**

- Define the most appropriate information resources.
- a. Value-added:  
**EURL ECVAM DB-ALM; AnimAlt-ZEBET**
  - b. Limitable (to a 3Rs-subset of documents) broad coverage: indicate what limitations you plan to use (e.g. MeSH-term-based: *animal use alternatives*).  
**EC-JRC ECVAM (<http://ecvam.jrc.ec.europa.eu>)(<http://tsar.jrc.ec.europa.eu>)**  
**US NICEATM-ICCVAM (<http://iccvam.niehs.nih.gov>)**  
**free internet: focus on specific web-sites, providing information also on validated alternative testing methods, e.g. AltTox.org (<http://www.alttox.org/>), Altweb <http://altweb.jhsph.edu/>**
  - c. Unlimited broad coverage.  
**free internet (access by ...)**

*NOTE* For basic research PubMed/Medline is often the preferred limitable broad coverage resource under b.). But for regulatory toxicity testing, PubMed/Medline is often not the resource of choice to find suitable validated alternatives, with EURL ECVAM, ICCVAM or AltTox.org, Altweb being the preferred entry points often allowing relevant information to be obtained using a single simple text box.

*NOTE* Please refer to Section Information Resources – General Considerations of this volume (p. 28) for a fuller discussion of 3Rs information resources. Section Information Resources-Inventories (see p. 34 of this volume) presents lists and look up tables of those resources classified according to their subject coverage, their type, and to their features for the 3Rs. The second volume of the EURL ECVAM Search Guide<sup>1</sup> provides data sheets for each 3Rs information resource.

#### STEP 4. RELEVANT SEARCH TERMS

- X** Compile the search terms that best describe your scientific objectives and approach, and need for 3Rs information. Select terms with appropriate levels of specificity/breadth. Consider thesaurus terms, and advanced queries.
- Field of investigation:  
**toxicology, regulations, REACH, etc.**
  - Objectives:  
**toxicity testing, eye irritation, eye corrosion, corrosivity, eye damage, chemicals, etc.**
  - Methods/Models:  
**Draize eye test, rabbit eye test, in vitro, ex vivo, alternatives, alternatives procedures, etc.**

*NOTE* Please refer to Section Search Terms and their Use for a discussion of search term hierarchy and a list of possible 3Rs relevant terms.

#### STEP 5 START YOUR SEARCH WITH A SIMPLE QUERY IN A 3Rs SPECIFIC CONTEXT

- X** Start your search in value-added 3Rs sources, trying out different search terms within a simple query, and browsing through the inventory (classification scheme) if available.
- Enter the **EURL ECVAM DB-ALM URL** or the **AnimAlt-ZEBET** in the address box of your browser.
  - Enter "eye irritation" or "eye corrosion" in the simple search box (Free Text Search" in the **EURL ECVAM DB-ALM** or better select directly the "Methods Search" option from the top menu bar and chose the search parameters of interest; or "search for...in the text fields" at **AnimAlt-ZEBET**)
  - You will retrieve a list of documents on alternatives. The value-added databases **EURL ECVAM DB-ALM** and **AnimAlt-ZEBET** also offer the information necessary to decide which of the retrieved methods is best suited to be employed. The **EURL ECVAM-DB-ALM** also covers related information. Thus, you will have the information at hand to consider the suitability of the alternatives.
- X** Evaluate the documents retrieved. Is there information on alternative method(s) that are suitable to reach the scientific purpose of your approach, are there potentially better search terms?

*NOTE* Please refer to Section The Seven Golden Steps (page 92) to Successful Searching for explanation why to start your search in a 3Rs specific context. Please refer to the Volume Information Resources: Data Sheets for the **EURL ECVAM DB-ALM** and the **AnimAlt-ZEBET** URLs.

*NOTE* To retrieve all available alternative methods in **AnimAlt-ZEBET** enter the topic definer term "animal testing alternatives" in the simple search box. Then, all provided methods will be listed and you can just skim through this "inventory", whereas the **EURL ECVAM-DB-ALM** provides Thematic Reviews of in vitro techniques for toxicity assessments related to chemicals with their related information. Validated/regulatory accepted methods are easily searchable and an inventory is listed on the **EURL ECVAM** website select: "Method Validation".

You already have sufficient information at this point. There are several validated/regulatory accepted alternatives to the Draize rabbit eye test and the data on eye corrosion are accepted by EU regulators – but they may not be suitable for assessing all physicochemical classes of test material. If a suitable alternative is not provided by these resources, go on to Step 6.

**STEP 6 LIMIT SEARCH RESULTS FROM MORE EXTENSIVE RESOURCES**

- If no information on suitable alternatives is found using the value-added sources, continue your search using limitable broad coverage sources.  
**Resource is the internet; you should follow specific link-lists from the “global clearing-houses” of information on alternative methods.**
- Try out different kinds of 3Rs-relevant limitations (e.g. MeSH-term-based, journal-based etc) to limit the results to relevant and manageable lists of documents. Evaluate the results and consider if it is possible to improve your query by adding varying search terms and Boolean operators.
1. Enter the [AltTox.org](http://AltTox.org) URL in the address box of your browser.
  2. Enter “eye corrosion” in the simple search box (“search ... Go”)
  3. You will retrieve a list of documents that are possibly relevant.
  4. Just choose the first one - 1. Eye Irritation/Corrosion (Web Pag; Fri Mar 04 08:37:00 CST 2011)
  5. There, a table of “Validated Non-animal Alternatives” is provided and additionally some background information. Many will, obviously, refer to ECVAM and ICCVAM websites where supplementary documents are made available. Anyway, you will also need to collect further information from documents which are freely available from the internet (e.g. Draft OECD Test Guidelines) to consider the suitability (links are provided).
- Evaluate the most relevant documents retrieved.

*NOTE* See Note to Step 3. Of course, you can also start at the **AltWeb-Portal**.

Again you may have all the information you need. You know, there are several validated/regulatory accepted alternatives to the Draize rabbit eye test and the data on eye corrosion will be accepted by EU regulators – but they may not be appropriate for all physical chemical classes of test materials.

Let us assume the “global clearing-houses” cannot show you the way to suitable alternatives: in that case you would go on with Step 7.

**STEP 7 BROADEN THE SEARCH HORIZON**

- If no suitable alternative was retrieved by restricting the search by predetermined 3Rs-relevant limitations, repeat step 5 in broader coverage resources with more general limitations consistent with your scientific methodology and objectives.  
**Access the internet via any search engine. Combine search terms with operators and try to limit the resulting document list without losing relevant information.**
- Again, evaluate the retrieved documents.

*NOTE* See Sections Basic Search Principles and Sections Search Terms and their Use for details on how to choose search terms and how to combine them with operators.

## POTENCY TESTING OF BOTULINUM TOXIN

### Background

The **bacterium Clostridium botulinum** produces some of the most potent known **neurotoxins**. They specifically and selectively block neurotransmitter release at the presynaptic membranes of motor nerves and thus cause paralysis of voluntary muscles. Seven types or serotypes of toxin (A, B, C, D, E, F, and G) are distinguished. Botulism in humans is associated with serotypes A, B, and E toxins while toxin types C and D affect animals.

Natural outbreaks are rare but result in a high death rate. Botulism is most often associated with eating food containing the toxin.

Botulinum toxin A is produced commercially for medical purposes.

Preventive **food hygiene, diagnostic procedures, and increasing therapeutic use** of toxins and antitoxins require rapid, efficient and sensitive methods for detection and identification of serotype as well as for potency testing of therapeutic products.

The standard method for botulinum toxin potency testing is the mouse Lethal Dose 50 (LD50) assay set out in the **European Pharmacopoeia 7.2 Monograph 2113 “Botulinum Toxin Type A for Injection”** (07/2011:2113, 3613-3615, 2011) and **Monograph 2581 “Botulinum Toxin Type A for Injection”** (07/2011:2581, 3615-3616, 2011). Alternative methods mentioned in the monograph: once they are scientifically validated for a particular therapeutic product with respect to the mouse LD 50 assay they may be used instead of the mouse test.

### Scenario

A company is going to establish commercial production of a botulinum toxin product: that will require potency testing of active substance. The company needs to assess the availability and validation status of potential suitable alternatives to the mouse LD50 assay.

**STEP 1. INFORMATION NEED**

- Clearly define your specific information need:  
**Are there alternative methods for product potency testing of botulinum toxin?**

*NOTE* Please refer to Section The Seven Golden Steps (page 92) for a discussion of various needs for information retrieval during the planning and the application of a project that involves the use of animals.

**STEP 2. COMPONENTS OF YOUR APPROACH**

- Identify the fundamental components of your scientific approach.
- a. Field of investigation:  
**potency testing of particular therapeutic products**
  - b. Specific objective(s):  
**determination of Botulinum toxin A activity for every new batch during and at the final stage of the production process**
  - c. Methods/Models:  
**Mouse lethal Dose 50 (LD50) assay**

*NOTE* It is important to narrow down your search to potency testing to determination of Botulinum toxin A activity. Food hygiene or diagnostic procedures are not relevant.

**STEP 3. APPROPRIATE INFORMATION RESOURCES**

- Choose the most appropriate information resources.
- a. Value-added:  
**AnimAlt-ZEBET**
  - b. Limitable (to a 3Rs-subset of documents) broad coverage: indicate what kind of limitation you plan to use for b. (e.g. MeSH-term-based: *animal use alternatives*).  
**Bibliographic Databases: MEDLINE, BIOSIS Previews, EMBASE**  
**Organizations: AltTox, Altweb, EURL ECVAM, ICCVAM, NC3Rs, etc.**
  - c. Unlimited broad coverage.  
**free internet access by...**

*NOTE* Please refer to Section Information Resources – General Considerations of this volume (page 28) for a fuller discussion of 3Rs information resources. Instead the Section Information Resources-Inventories (see page 34 of this volume) presents lists and look up tables of those resources classified according to their subject coverage, their type, and to their features for the 3Rs. The second volume of the ECVAM Search Guide' provides data sheets for each 3Rs information resource.

*NOTE* Appropriate databases for your search are MEDLINE as well as the fee-based databases BIOSIS Previews and EMBASE.

#### STEP 4. RELEVANT SEARCH TERMS

- Compile the search terms that best identify your scientific approach as well as the aspect of the 3Rs.  
Consider terms with varying levels of specificity/breadth.  
Consider thesaurus terms, and advanced queries
- a. Field of investigation:  
**potency testing, biological products, drugs, biologicals, etc.**
  - b. Objective(s):  
**Clostridium botulinum, Clostridium botulinum toxin A, toxin, botulism, etc.**
  - c. Scheduled Methods/Models:  
**Mouse Lethal Dose 50 assay, LD50 assay, alternatives, alternatives procedures, in vitro, cell culture, humane endpoints, etc.**

*NOTE* Please refer to Section Search Terms and their Use for a discussion of search term hierarchy and a list of possible 3Rs relevant terms.

#### STEP 5 START YOUR SEARCH WITH A SIMPLE QUERY IN A 3Rs SPECIFIC CONTEXT

- Start your search in value-added 3Rs sources, by trying different search terms within a simple query and browsing through the inventory (classification scheme) if available.
1. Enter the AnimAlt-ZEBET URL in the address box of your browser.
  2. Enter "clostridium botulinum" in the simple search box ("search for ... in text fields")
  3. You will retrieve a list of alternatives. The value-added databases AnimAlt-ZEBET offers information on the suitability of the alternatives.
- Evaluate the retrieved documents:  
Is there sufficient information on alternative method(s) that are suitable to reach the scientific purpose of your approach?

*NOTE* Please refer to Section The Seven Golden Steps (page 92) for explanation why to start your search in a 3Rs specific context.

Do not forget to always consult the EURL ECVAM website, sector "Method Validation" to investigate whether there are validated approaches available".

Please refer to Section Information Resources: Datasheets for the EURL ECVAM website and AnimAlt-ZEBET URL.

You have already sufficient information. There are several alternatives to the LD 50 test developed and published. However, they have to be suitable for validation for a particular product with respect to the LD 50 assay.

If a suitable alternative is not provided by this resource, you will go on with Step 6.

**STEP 6 LIMITATION OF SEARCH RESULTS FROM EXTENSIVE RESOURCES**

**X** If no suitable alternative is detected within the value-added set of documents, go on with your search in limitable broader coverage resources.

**Resource is MEDLINE.**

**X** Try out, different kinds of 3Rs-relevant limitations (e.g. MeSH-term-based, journal-based etc) to limit the results to relevant and manageable lists of documents. Evaluate the results and improve your query by adding varying search terms and Boolean operators.

**1. Enter the PubMed URL in the address box of your browser. PubMed is one of the interfaces for search MEDLINE.**

**2. You have preselected search terms, e.g. "Clostridium botulinum" and "alternatives", see Step 4.**

**3. You decided to use the MeSH-term-based search offered by PubMed.**

**4. Click on "MeSH-Database". Type in your preselected search terms. It will lead you to preferred MeSH terms. Select and transfer appropriate terms to the search box. Finally click on "Search PubMed" to perform the search "Clostridium botulinum"[Mesh] AND "Animal Use Alternatives"[Mesh].**

**5. Search results are shown as a list of publications that are quite relevant.**

**X** Evaluate the most relevant of the retrieved documents.

*NOTE* See Notes to Step 3. Of course, you can also search the fee-based databases BIOSIS Previews or EMBASE. In addition, you can extend your search, as previously indicated, to websites, e.g. ECVAM or NC3Rs selected in Step 3.

*NOTE* Please refer to Section Basic Search Principles for explanations of basic search principles. Please keep in mind that every database search engine or Internet search engine predetermines certain rules on how to search.

You may already have sufficient information. Several publication and reports are retrieved in bibliographic databases and on websites. Let us assume searches in broad coverage resources such as the bibliographic database MEDLINE and ECVAM or the NC3Rs website cannot provide you the information you are looking for. Then, you would go on with Step 7 because they might focus on other areas of alternative methods.

**STEP 7 BROADEN THE SEARCH HORIZON**

**X** If no suitable alternative was retrieved by restricting the search by predetermined 3Rs-relevant limitations, repeat step 5 in broad coverage resources with more general kinds of limitation, that comply with your scientific expertise and objectives. **Access the internet via any search engine. Combine search terms with operators and try to limit the resulting document list without losing relevant information.**

**X** Again evaluate the retrieved documents.

*NOTE* See Section Basic Search Principles and Search Terms and their Use for details on how to choose search terms and how to combine them with operators.



- Annex I of the EURL ECVAM Search Guide summarises some of the legal background to current Information Requirements on alternative methods in the EU.
- Making proper use of all sources of information on alternative methods is a key part of preparing, evaluating and managing research projects in the life sciences if they are to comply with these legal requirements.
- The provisions of the new Directive 2010/63/EU on the protection of animals used for scientific purposes make it even more important to intensify efforts for improving search procedures that efficiently and effectively target information on alternative methods to animal experiments in the life sciences.

## LEGAL BACKGROUND OF INFORMATION REQUIREMENTS

The European Union has legislation protecting animals used for experimental and other scientific purposes: these impose legal requirements to identify and use all appropriate methods to replace, reduce and refine such animal use. Finding relevant information plays a key part in discharging these obligations.

In March 1986, the Member States of the Council of Europe agreed the “**European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes**” (71), recognising that “man has a moral obligation to respect animals and to have due consideration for their capacity for suffering and memory”. The Convention acknowledges animal experiments are necessary; but seeks to replace animal experiments, to minimise pain and animal suffering, and to reduce the number of animals used.



The European Commission enacted the “**Council Directive 86/609/EEC** 24 November 1986 on the approximation of laws, regulations, and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes”. (1)

**In September 2010, the European Parliament adopted the new Directive 2010/63/EU on the protection of animals used for scientific purposes that further reinforces the application of the 3Rs.** Any production, use and care of animals for scientific procedures must satisfy the internationally recognised principles of *replacement, refinement and reduction*. *Refinement* shall apply to the care, accommodation and breeding of animals. The Directive makes legislative provision for the 3Rs principally in *Recitals 10-13* and *Articles 1, 4 and 13*. Consequently, **Directive 2010/63/EU** introduces the requirement to evaluate projects for their compliance with these principles (*Article 36 ff*). Development, validation and use of alternative approaches have become a strict legal requirement and the requirement for provision, dissemination and the use of information is referenced in various places throughout the entire Directive. **This new Directive comes into force on 1 January 2013.** (77)

*Article 4 - Principle of replacement, reduction and refinement:*

- **Replacement Alternatives** - Article 4(1)  
“Member States shall ensure that, wherever possible, a scientifically satisfactory method or testing strategy, not entailing the use of live animals, shall be used instead of a procedure”.
- **Reduction Alternatives** - Article 4(2)  
“Member States shall ensure that the number of animals used in projects is reduced to a minimum without compromising the objectives of the project.”
- **Refinement Alternatives** - Article 4(3)  
“Member States shall ensure refinement of breeding, accommodation and care, and of methods used in procedures, eliminating or reducing to the minimum any possible pain, suffering, distress or lasting harm to the animals.”

To meet the legal obligations set out in the new Directive scientists, and regulators, need to consult scientific literature prior to any experimental study using laboratory animals, and identify and apply all relevant 3Rs strategies and methods. Making full use of all sources of information on alternative methods is a key part of **preparing research projects** (Article 37, Annex VI and Article 38 (2)(b)) in the life sciences in compliance with the EU legislative requirements.

## INFORMATION REQUIREMENTS OF NATIONAL LAWS

From 1<sup>st</sup> January 2013, European Member States will be required to comply with the provisions of Directive 2010/63/EU including the implementation of a formal project evaluation and authorisation processes (Articles 36-45). In the past, national legislation based on the (previous) Directive 86/609/EEC - and Article 24 in particular, were, however, entitled to retain stricter measures for the protection of animals used in experiments providing they do not distort the internal market.

- **Although national approval and authorization procedures for animal experiments differ in detail, they must all conform to the 3Rs principle specified in Article 4 of the Directive 86/609/EEC.** Replacement alternatives must be used if available, and animal use must incorporate available reduction and refinement opportunities. Animal experiments are limited to those strictly necessary.
- **Scientists are responsible for providing information** to demonstrate these requirements are being met. They have to supply information on the justification for the planned animal experiment, including information on non-availability of suitable alternative methods. In order to do so efficiently and effectively scientists and others must know where to look and how to find relevant information.
- **Generally the information supplied by the scientists as part of the project evaluation and authorisation processes is evaluated by local ethical review process and/or the national competent authority** before a planned experiment or programme of work is approved or authorised. Typically national laws do not prescribe how scientists compile or archive this information.

In practice, the information requirements are determined, directly or indirectly, in national legislation or guidelines as outlined with the United Kingdom Animals Scientific Procedures Act.

**The United Kingdom** “Animals (Scientific Procedures) Act 1986” (as amended 2012) stipulates that all animal use must be authorised and licensed. In Great Britain project licences are issued by the Home Office. (74) Protected animals include all “living vertebrates other than man, and cephalopods. Protection of vertebrates is extended to immature forms (foetal, larval or embryonic form) when they reach two-thirds way through the gestation of incubation period. Scientists must supply exceptional justification to use animals of higher species.

Scientists who apply for project licences are responsible for providing the authorities with documentation demonstrating that alternatives to the animal experiments have been properly researched and considered and that the proposed animal use does not unnecessarily duplicate previous experiments.

Applicant must supply detailed protocols including endpoints and severity limits, and confirmation that the application has successfully completed a local ethical review process. Applications are assessed by Home Office inspectors.

## IMPORTANT STEPS TOWARDS ENHANCED ANIMAL PROTECTION IN THE EU

### Recognition of Animals as Sentient Beings

In 1997, the “**Treaty of Amsterdam**” made substantial changes to improve the protection of animals in the EU. (73) The EU Member States adopted a legally binding “Protocol on the Protection and Welfare of Animals”, annexed to the Treaty, which **for the first time recognised animals as sentient beings rather than goods or property, and are deemed capable of feeling pain and of suffering**. The “Protocol on Protection and Welfare of Animals” thus creates an obligation for the Community and the Member States to pay regard to the welfare of animals in formulating and implementing the Community's agriculture, transport, internal market, and research policies.

### The New Directive on the Protection of Animals Used for Scientific Purposes

In line with the EC Treaty's “Protocol on Protection and Welfare of Animals”, and to better reflect obligations entered into when the European Commission signed and ratified Council of Europe Convention ETS123, in 2002 the process of revision of the Council Directive 86/609/EEC began. From the beginning, scientific experts were involved in the preparations for the revision. In 2006, the Commission held a public consultation on the revision of Directive 86/609/EEC. In November 2008, the Commission published a “Proposal for a Directive of the European Parliament and of the Council on the Protection of Animals used for Scientific Purposes”. Finally, in September 2010, the European Parliament adopted the revised Directive on the protection of animals used for scientific purposes. (77)

The final text was published in the Official Journal of the European Union in October 2010. **The provisions of Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes will take effect on 1 January 2013.** (77).

The new Directive **improves and harmonises the standard of protection of animals** used in scientific procedures in accordance with our current understanding of the animal welfare issues.

Article 4 of the new Directive emphasises explicitly the principle of replacement, reduction, and refinement developed by Russell and Burch (1959) (2), which is an internationally accepted approach to minimise the use of laboratory animals.

The Directive 2010/63/EU provides **mandatory procedures regarding the authorisation and evaluation of animal experiments, and the minimum information requirements to assess a project's compliance with the requirements of the 3Rs**. Article 37 of the Directive specifically requires that applications for animal experiments' authorisation shall include **information on the elements set out in Annex VI covering application of methods to replace, reduce and refine the use of animals**.

The changes to the EU legislation on the protection of animals used for scientific purposes has made it even more important to intensify efforts for improving search procedures that efficiently and effectively target information on alternative methods to animal experiments in the life sciences.

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## LIST OF ACRONYMS

<b>A</b>	<b>AATEX</b>	Alternatives to Animal Testing and Experimentation
	<b>AGRICOLA</b>	Agricultural Online Access
	<b>AGRIS</b>	Agricultural Information System
	<b>ALTBIB</b>	Bibliography on Alternatives to the Use of Live Vertebrates in Biomedical Research and Testing
	<b>ALTEX</b>	Alternatives to Animal Experimentation
	<b>Altweb</b>	Alternatives to Animal Testing on the Web
	<b>ATLA</b>	Alternatives to Laboratory Animals
	<b>ATW</b>	Animal Technology and Welfare
	<b>AWIC</b>	Animal Welfare Information Center
<b>C</b>	<b>CAAT</b>	Johns Hopkins Center for Alternatives to Animal Testing
	<b>CARDAM</b>	Centre for Advanced Research & Development on Alternative Methods
<b>D</b>	<b>DB-ALM</b>	DataBase service on ALternative Methods to animal experimentation of EURL ECVAM
	<b>DHT</b>	Dr Hadwen Trust
	<b>DIMDI</b>	German Institute of Medical Documentation and Information
	<b>DOAJ</b>	Directory of Open Access Journals
<b>E</b>	<b>EC</b>	European Commission
	<b>EURL ECVAM</b>	European Union Reference Laboratory for Alternatives to Animal Testing
	<b>ECEAE</b>	European Coalition to End Animal Experiments
	<b>ecopa</b>	European Consensus-Platform for Alternatives
	<b>EMBASE</b>	Excerpta Medica Database
	<b>EPAA</b>	European Partnership for Alternative Approaches to Animal Testing
	<b>ESTIV</b>	European Society of Toxicology In Vitro
	<b>EU</b>	European Union
	<b>eurca</b>	European Resource Centre for Alternatives in Higher Education
<b>F</b>	<b>FRAME</b>	Fund for the Replacement of Animals in Medical Experiments
<b>H</b>	<b>HSUS</b>	Humane Society of the United States
<b>I</b>	<b>ICCVAM</b>	Interagency Coordinating Committee on the Validation of Alternative Methods
	<b>IHCP</b>	Institute for Health and Consumer Protection (IHCP)
	<b>IIVS</b>	Institute for In Vitro Sciences
	<b>ILAR</b>	Institute for Laboratory Animal Research Journal
	<b>InterNICHE</b>	International Network for Humane Education
	<b>IVTIP</b>	In Vitro Testing Industrial Platform
<b>J</b>	<b>JAS</b>	Journal of Animal Science
	<b>JAAWS</b>	Journal of Applied Animal Welfare Science
	<b>JACVAM</b>	Japanese Center for the Validation of Alternative Methods
	<b>JRC</b>	Joint Research Centre
	<b>JSAAE</b>	Japanese Society for Alternative to Animal Experiments
	<b>LAD</b>	Laboratory Animal Refinement Database
<b>M</b>	<b>MEDLINE</b>	Medical Literature Analysis and Retrieval System Online
	<b>MeSH</b>	Medical Subject Headings

<b>N</b>	<b>NALT</b>	National Agricultural Library Thesaurus
	<b>NC3Rs</b>	National Centre for the Replacement, Refinement and Reduction of Animals in Research
	<b>NKCA</b>	Netherlands Knowledge Centre on Alternatives to Animal Use
	<b>NORINA</b>	Norwegian Inventory of Audiovisuals
<b>P</b>	<b>PED</b>	Environmental Enrichment for Primates – Primate Enrichment Database
	<b>PMC</b>	PubMed Central
<b>R</b>	<b>REACH</b>	Registration, Evaluation, Authorisation and Restriction of Chemicals
<b>S</b>	<b>STN</b>	Scientific & Technical Information Network
<b>T</b>	<b>tpa</b>	tons per annum
	<b>TSAR</b>	Tracking System for Alternative test methods Review, Validation and Approval in the Context of EU Regulations on Chemicals
<b>U</b>	<b>UCCCAA</b>	UCDavis Center for Animal Alternatives Information
	<b>UFAW</b>	Universities Federation for Animal Welfare
	<b>URL</b>	Uniform Resource Locator
<b>Z</b>	<b>ZEBET</b>	Centre for Documentation and Evaluation of Alternatives to Animal Experiments
	<b>zet</b>	Centre for Alternative and Complementary Methods to Animal Testing

ves The ECVAM Search Guide for Untrained Database Users Good Search Practice on Animal Alternatives The ECVAM Search Guide for Untrained Database

**M**aking full use of all sources of information on alternative methods is a key part of preparing research projects in the life sciences using laboratory animals in compliance with the EU legislative requirements. A major challenge to locate relevant high quality information about a proposed field of scientific investigation is the exponential increase of scientific publications in the recent past. Over the last years the electronic resources, originally developed to offer a potential solution to this problem, have shown a similar proliferation. The question arises: how best to search information specifically on the 3Rs (replacement, reduction, refinement of animal use) in the World Wide Web that is heterogenic, constantly changing and growing?

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