Conducting a search for alternatives

BACKGROUND

The ability to access and implement information on the Three Rs (Replacement, Reduction and Refinement) is essential for ethical and scientific reasons, because it can lead to improvements in animal welfare and scientific outcomes, as well as to saving resources. It can prevent unnecessary duplication of studies, improve experimental design, and ensure that existing and new alternative methods are used as widely as possible.

In addition, the new EU *Directive 2010/63/EU* on the protection of animals used for scientific purposes, stipulates that the principles of the Three Rs should be implemented and that project evaluation should assess compliance with this requirement. It also includes the condition that EU Member States should contribute to development and evaluation of alternative approaches, including promotion of those approaches and dissemination of any related information. Therefore, it is important to consider whether Three Rs information is readily available and whether scientists are effectively accessing it.

AIM

To help scientists effectively to find and make use of all Three Rs information relevant to their proposed experimental study, this guide provides an introduction to the basic principles of searching for such information. It assumes no previous knowledge of search techniques or of the facilities available for obtaining information from the Internet. It acts as a starting point for scientists, giving advice on terminology, correct strategies and available resources for efficiently conducting internet-based searches. When further in-depth or specific guidance is available this is highlighted and links are provided.

STRUCTURE

The guide is presented as a series of pages, listed below under **What information is offered here**?, and accessible from links found there. Some of the links are internal, leading to other pages in the guide; others are links to external websites.
Although every effort is made to ensure all links are up-to-date we welcome any suggestions for new, relevant ones and feedback if any are found to be unreachable.
You may find it useful to add some of these links to your own bookmarks. That can be done by right-clicking on the link and selecting "add to favourites" or "add bookmarks", depending on the browser used.

WHAT INFORMATION IS OFFERED HERE

SEARCH BASICS

Basic principles applying to the construction of search filters for use on Internet search engines or on any on-line database are described here. This includes general considerations relating to the choice of search terms and to the use of operators to define the links between the terms.

CONDUCTING A SEARCH

This section focuses on performing a literature search in bibliographical databases but much of the information will be applicable to search engines. It provides suggestions for how to approach and report a search on the Three Rs, including a list of terms relating to reduction, refinement and replacement and information on maximising the number of relevant papers you find.

MAILING LISTS AND DISCUSSION FORUMS

A comparison of selected Internet search engines and meta-searchers, including what to consider when choosing which one. It can be difficult to retrieve Three Rs information from traditional bibliographic databases, because scientific publications generally do not include specific details about procedures, animals and husbandry in their titles or abstracts. Another way to find such information is by making less formal enquiries to other scientists and/or technicians, so this section gives a description of Internet resources for enabling such peer-peer communication. to use.

FREE DATABASES

A description of some of the databases which can be freely accessed from the Internet, together with brief guide notes on how to perform searches within some of these databases.

ACCESSING THE INVISIBLE WEB

This section provides information regarding specialised resources that make it easier to access the 'Invisible Web' (also referred to as the 'Deep Net', 'Deep Web'or 'Hidden Web'), which is the part of the Internet that is not searched by standard search engines (e.g. subscription databases requiring registration and sources containing documents in formats that are not accessible to the common search engines).

EXTERNAL LINKS

Useful links to external resources and literature of relevance to the Three Rs, searching, sharing information and to the use of the Internet.

This section focuses on performing a literature search on bibliographic databases. However, some of the general principles, and the list of search terms relating to the Three Rs could be applicable to searches carried out on Internet search engines. It includes information on planning a search, designing a search strategy, defining search terms including examples of subject-specific terms, and how to report your search.

PLANNING A SEARCH

It is essential that a literature search is an integral first step in the planning of any research programme. Scientists should critically review previous literature to check if their proposed research is novel, to determine how previous similar studies were conducted, find the severity of the procedures, and identify all feasible methods of testing the hypotheses in the planned programme (see the FRAME Strategic Planning Poster) .

In recent years systematic reviews of animal-related research have been advocated as a robust method of conducting such literature searches. A systematic review (SR) is a literature review focussed on a single question which tries to identify, appraise, select and synthesise all available high quality research evidence relevant to that question. Whether you adopt a systematic or more traditional literature review many of the principles are the same and should result in direct implementation of the Three Rs. A robust literature search can reveal gaps in knowledge, and identify which model will give the best answer to the research question, including if an animal is absolutely necessary (Replacement). It can highlight new techniques that might be less invasive or have more humane endpoints (Refinement) and help to identify effective experimental designs and prevent unnecessary duplication of animal experiments (Reduction).

Leenaars et al (2012) provide a useful overview of the five basic steps that need to be addressed when planning a comprehensive search:

1. Formulate a focussed research question
2. Identify appropriate databases and sources of studies
3. Transform the research question into a search strategy
4. Collect search results and remove duplicates
5. Identify potentially relevant papers
For further details see their paper [Leenars et al]

DESIGNING A SEARCH STRATEGY AND DEFINING SEARCH TERMS

When you have formulated your research question and identified appropriate databases then you need to design a search strategy that will enable you to address your research question. Designing a search strategy for a specific database can be complex and depends upon specific search terms, the search capabilities of the database and the indexing system it uses. It may be necessary to take a specific course in the use of the major electronic bibliographic databases, which may be available at an institutions library or to involve a specialist from the library for advice when developing a comprehensive search strategy.

Leenaars *et al* (2012) provide a very good breakdown of how to transform a research question into a search strategy for PubMed, which is a very good introduction for this database. The following are general considerations when designing a search strategy.

Initially, it is necessary to define search terms specific to the field of study and the research topic. How to identify these is described below. The terms then need to be combined into a search filter using Boolean or other operators.

The use of parentheses and operators makes it possible to construct very long and complicated search filters, which include the whole of the desired search. However, on systems which permit the storage and subsequent recall of individual search sets, it is better to do the search in a number of steps, each dealing with one concept, and then to combine the retrieved sets in various ways. This makes it easier to go back and adapt the various filters if necessary since it is possible to see how many documents are being retrieved by each part of the search strategy. Always make notes on which combinations of which sets are being used at each stage, because if the search ends up including many steps it is sometimes quite difficult to remember exactly what was done in the earlier steps and to identify which sets to use again in order to refine the search. It is also useful to copy and save the search filters that you have designed for use in future search strategies and for reporting your search. (See *Reporting searches* below.)

If the first search retrieves too many documents, of which many are irrelevant, it will be necessary to make the search filter more precise. Do this by using narrower terms, for example searching on "rats" instead of "rodents". Another trick is to limit the search on the most important terms to the title field, if that is permitted.

On the other hand, the first attempt may retrieve very few documents. In this case, some of the very specific parts of the search profile should be removed and/or broader search terms should be used. It may be possible to explode a search. This is possible on databases such as Embase and Medline which use a hierarchical indexing system. The policy of these databases is to assign the narrowest indexing term possible. For example, the Emtree system used by Embase has the index term "cell culture" and under this a number of terms describing specific types of cell culture.

A paper describing monolayer cultures will be indexed with the term "monolayer culture", while a paper describing cell cultures which are not listed among the more specific terms will be indexed with "cell culture". Therefore, searching on "cell culture" will not retrieve the documents on monolayer cultures if the search is limited to the descriptor field or, in the case of an all fields search, if the word cell does not appear in the abstract or title. Exploding the search term "cell culture" will retrieve all documents indexed with the terms listed below cell culture in the hierarchy. Therefore it will retrieve documents about monolayer cultures, but also those about fibroblast cultures, lymphocyte cultures, etc. Explosion may sometimes be useful, but it does entail the risk that a huge number of documents will be retrieved.

Having performed the subject-specific search, most scientists will want to obtain full copies of documents that appear relevant and go through these to see if the hypothesis is valid and if the proposed study is justified. This is a good opportunity to make notes of anything that might be relevant to the Three Rs, for example;

* Are there any references to *in vitro* studies?
* Has any work been done on less evolved species?

* Has a particular strain of animal been shown to be more sensitive to the effects that will be studied? If yes, it may be possible to obtain statistically meaningful results using fewer animals than if a less sensitive strain was used.
* Any anaesthetics and analgesics used in the studies should be noted. It may be advisable to perform a further search on the effects of these compounds, because some may cause physiological changes which will have a confounding effect on the results, while others may result in fewer adverse effects.
* Are there any statistical models that have been developed for use in this type of study and will these affect the design of the experiments?
* Is there any mention of possible refinements such as the use of less invasive procedures, different methods of handling the animals or attempts to provide environmental enrichment?

If any of the papers are found to be irrelevant then you must note down the criteria used to exclude them and how many papers were excluded under each criterion.
Either as part of or after this first analysis has been completed, a second search should be carried out to investigate further possibilities for replacement, reduction and refinement. The Three Rs cover a very broad set of concepts.

It is again necessary to consider using synonyms, acronyms, spelling variants and truncation. At this stage, it may be a useful exercise to limit each search filter to subject-specific keywords expressing only one concept and use some broader terms so as to extend the search into other disciplines. For the same reason, it is useful to try a search in a different set of databases.

As noted above at all stages, retrieval of relevant documents will be influenced by the indexing systems of the different databases and the extent to which the search is tailored towards those systems. Some database hosts such as ProQuest Dialog (requires Athens or institutional login [link to page]) permit a simultaneous search to be carried out across multiple databases. This can save a lot of time, but it is impossible to optimise the search strategy to the indexing system of each individual database. However, Dialog Bluesheets are available without a login. They are written guides for every database on the Dialog service, containing detailed instructions on search techniques for the special features of each database, including file description, subject coverage, date range, update frequency, sources of the data, and the origin of the information. Most importantly the search options section shows the field labels that you can use to focus or narrow your search, as well as examples of how to use them online.

Retrieving the full records of known relevant articles from the selected database will show the indexing terms that are used by that database.

SUBJECT-SPECIFIC TERMS

The best way in which to generate a list of subject-specific terms is to identify a set of core papers about the subject. A good place to start is by looking through some review journals.

Once one or two pertinent reviews have been found, these can be used to identify important papers and important authors in the field. This may result in some older references being listed. It can be useful to follow these forwards in time by using the Web of Knowledge [Web of Knowledge] citation index (requires Athens or institutional login), to identify articles which have cited these key papers and key authors. Relevant words can then be extracted from the full texts of the core papers, including any keywords supplied by the authors.

The types of search terms that need to be considered relate to the following categories:
• the field of interest: e.g. cardiology, pharmacology, neurology;
• the species used in the reported studies;
• the systems or anatomical structures that are studied;
• any pathological or physiological processes that might be involved;
• any hormones, enzymes or chemicals of interest or relevance to the study.

Try to include synonyms, for example, heart can be used in place of cardiac. Include any commonly-used acronyms, for example, GPT, NSAID. It is important to think of possible variants in spelling such as in the British and US spellings of tumour or foetus.

It would be useful at this stage to go into one or two databases and retrieve the full records for some of these core papers. This can easily be done by searching on appropriate words from the title and author names in the title and author fields, and/or searching by date in the year field. The full records will show the words which have been used to index the articles for the databases. They may help to identify some more keywords. If many of the core papers cannot be retrieved from a database, this will serve as an alert that this database is not going to be very useful for the planned search.

The indexing thesaurus should ideally be consulted, in order to obtain the preferred terms or indexing codes and also narrower and/or broader terms/codes for these concepts. Otherwise, attention once again has to be given to broader and narrower descriptions, possible synonyms, use of both singular and plural, likely usefulness of truncation and possible variations in spelling.

Hoojimans *et al* (2010) and de Vries *et al* (2011) have created a search filter for finding all animal studies in PubMed and Embase, respectively that can be copied and pasted into your search filter in addition to your subject-specific terms.

REPORTING SEARCHES

To demonstrate the systematic and robust nature of your search it is important to report/publish your search strategy whenever possible (this might be as a supplement to your scientific paper). This will facilitate dissemination of Three Rs information and aid other researchers to search effectively. Leenaars *et al* (2012) provide a good example of a diagrammatic way of presenting the main search results including exclusion criteria. You should also try to include your search filter. As a general rule when reporting the search you should include:

1. all databases and other sources searched
2. the dates of the last search for each database and the period searched
3. full search strategies (including all search terms/filters)
4. any language or publication status restrictions used
5. exclusion criteria

Whether publishing the search strategy or not it is important to save this information for your own future use.