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AWIC Tips for Searching for Alternatives to Animal Research and Testing

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The following guidelines were developed to assist researchers, information specialists, and Institutional Animal Care and Use Committee (IACUC) members, when conducting literature searches to determine if alternatives to the use of animals exist and whether a protocol unnecessary duplicates previous research. When searching for alternatives, the staff at the Animal Welfare Information Center (AWIC) refer to the tenets of the 3 R's introduced by W.M.S. Russell and R.L Burch (1959) in their book [The Principles of Humane Experimental Technique](#)([link is external](#))¹. The 3 R's represent reduction in the number of animals used, refinement of techniques and procedures that reduce pain and distress, and replacement of animal with non-animal techniques.

The first step in conducting a search for alternatives, involves communication between the investigator and the information specialist. The specialist cannot effectively search for alternatives without a basic understanding of the type of research the investigator is proposing. The most efficient means of communicating is a direct dialogue between the investigator and the information specialist. A third party should not be used to convey information.

Investigators can assist information specialists by being prepared to give precise and specific information about their research or testing procedures. The following may serve as a guideline for the type of information the investigator may be asked to provide:

1. What is your general area of study (e.g., cardiology, neurology, toxicology, etc.)?
2. What species are you currently working with (e.g., rats, dogs, swine, etc.)?
3. Briefly describe your experimental protocol.
4. What specific systems or parts of the anatomy are involved (e.g., central nervous system, brain stem, parabrachial nucleus)?
5. Please give correct spellings of these structures and any acronyms (e.g., CNS, PBN). European spellings are important as well.
6. If you are studying the effects of a particular hormone, enzyme, or chemical agent, please give the complete spelling of the compound as well as its trade name and acronym (e.g., bovine somatotropin, BST).
7. Do you know of any prominent authors in your area of research? Have you published any previous literature that relates to your current study?
8. What makes your study unique from previous studies (e.g., testing a new technique, investigating a new compound, further understanding of a biochemical pathway)?
9. Are you aware of any possible alternatives to your research, such as experiments conducted on alternative species, cell culture, or in vitro studies?
10. Have you had any other searches conducted for you? If so, what databases were used (e.g., MEDLINE, AGRICOLA, BIOSIS)?
11. What keywords were used (e.g., kidney, parathyroid hormone)?
12. What years were searched (e.g., 1995-present)?

As with any type of searching, success in retrieving relevant citations will depend directly on the quality of the information provided.

Search Strategy

Once the initial exchange of information has taken place, the information specialist can begin to formulate a search strategy. Search strategies for alternatives may be divided into two phases, reduction and refinement, and replacement.

Phase I (Reduction and Refinement)

Phase I consists of a generalized database search used to retrieve citations pertinent to the investigator's field of study. Citations retrieved during this phase, should provide information on current research, alert the investigator to whether or not they are performing duplicative studies, and possibly provide information to refine experimental techniques.

During Phase I, the information specialist and/or researcher may find it helpful to develop search strategies using research databases available for free on the internet (i.e. AGRICOLA, MEDLINE, TOXLINE) or available through their institutions' networked resources. Most academic and public library's websites contain a link to a page entitled "Databases." Following this link the user will usually be provided with descriptions of the databases available and instructions on how to access these databases using accounts provided by their institution. Most will require a student, faculty, or patron login. United States Department of Agriculture (USDA) employees and contractors may wish to

explore and develop search strategies using databases available through USDA's Digital Desktop Library (DigiTop) using their government login.

Library web pages and the corresponding databases available through different platforms from these sites, are highly variable from institution to institution. If the institution offers self paced tutorials and/or training workshops it is advisable for researchers and information specialists to receive training on the tools available to them through their local library. Using "free" and/or institutional resources with yearly subscriptions offers the information specialist and researcher the freedom to experiment with keywords, explore indexes and thesauruses, and read abstracts. If the investigator has published previous literature this is a good time to read abstracts of his or hers previous work and become familiar with terminology used to describe the study and to note what terms were used to index the abstract. At this point the information specialist should have a general idea of how much literature exists on a specific topic. If few relevant citations are found, the information specialist may need to broaden the search strategy or use the expanded capabilities of online database searching to develop the search. If hundreds of citations are retrieved using only a few years worth of bibliographic data, then it is necessary to further consult with the investigator on ways to narrow the search.

When searching for alternatives, information specialists should search multiple databases. A multidisciplinary approach to searching may yield surprising results particularly for individuals who are not accustomed to searching the literature outside their general area of study, (e.g., Medicine). AWIC provides [links and descriptions of databases](#) providing information on biomedical research, biological science, animal science, veterinary medicine, fish and wildlife research, toxicology and specialized alternative methods.

Many of these databases are available free on the web, while others are fee based and available via vendor, such as DIALOG, OVID, EBSCO, CSA, DIMDI, Elsevier Science, ProQuest, Silverplatter, STN and Thompson Reuters. Our recommendation is to find a vendor that provides you with one platform to search the most databases that are pertinent to your research, as well as the 3Rs of alternatives - Refinement, Reduction and Replacement. If you have any questions, please contact your library or AWIC.

Phase II (Replacement)

Upon completion of Phase I, the information specialist should have a basic understanding of the research area including: 1) the literature published in the particular field, 2) the techniques used, and 3) the commonly used species. The information specialist is now ready to search for possible replacement alternatives.

The following questions may be used to assist in the search for replacement alternatives:

1. Are there in vitro techniques that may reduce or replace the number of animals used (e.g., chorioallantoic membrane assay, use of primary cultured hepatocytes)?

2. Are there any alternative animal models (e.g., invertebrates, fish, protozoa, etc.)?
3. Have any computer simulations or statistical models been developed that relate to the study?

When searching for alternatives, information specialists should search multiple databases. A multidisciplinary approach to searching may yield surprising results particularly for individuals who are not accustomed to searching the literature outside their general area of study, (e.g., Medicine). AWIC provides information about a number of useful [databases](#) that cover the topic areas of biomedical research, veterinary medicine, and animal science.

"Animal testing alternatives" is a phrase used to index citations regarding alternatives in the AGRICOLA, MEDLINE, TOXLINE, CANCERLIT, CAB Abstracts, and BIOSIS PREVIEWS databases. However it is not used to index alternative studies in other databases such as EMBASE and LIFE SCIENCES. Although useful, this phrase should never be the only strategy used to retrieve information on alternatives. Depending on the study, other terms such as tissue culture, cell culture, in vitro, simulation, model, refinement, reduction, or alternative may be used. For a listing of terms that may be helpful when conducting alternative searches information specialists may refer to [Animal Welfare Information Center Scope Notes](#).

It is important to keep in mind that although electronic databases are powerful resource tools, most databases do not index journals before the mid-sixties and relevant information from early studies will not be retrieved. In addition, information on alternatives is available in newsletters, books, and proceedings, which not all databases index.

Sample Search for Alternatives

The following is an actual search that was requested by an IACUC member and a description of the steps that the AWIC information specialist performed. The IACUC member requested a search for alternatives to the use of zona free hamster oocytes to test human sperm penetration, motility, and viability.

After initial information was exchanged about the protocol, a list of keywords was developed. The specialist then conducted a brief initial search using the National Agricultural Library's DigiTop Navigator platform to become familiar with abstracts in which human sperm penetration, motility, and viability were tested. Databases currently available in Navigator include: AGRICOLA, AGRIS, BIOSIS, CAB Abstracts, Fish, Fisheries & Aquatic Biodiversity Worldwide, Food Science and Technology Abstracts, GEOBASE, GeoRef, MEDLINE, Wildlife & Ecology Studies Worldwide, and Zoological Record.

The specialist was aware that extensive tests have been developed to assess semen characteristics in domestic farm species and therefore contacted a farm animal reproductive physiologist for further information. The physiologist confirmed that alternative methods exist to test bovine and human sperm penetration such as a variety of cervical mucus tests. Based on this information the specialist developed the following search strategy.

Databases Selected

After initial searching was completed seven different biological and medical databases were selected and searched including AGRICOLA, MEDLINE, CAB ABSTRACTS, BIOSIS PREVIEWS, CSA LIFE SCIENCES ABSTRACTS, EMBASE and ELSEVIER BIOBASE.

Search Strategy

Set	Items*	Description
1	4064598	(SPERM? OR SEMEN?)
2	2884725	(MOTIL? OR VIABIL? OR MORPHOL?)
3	443418	S1 AND S2
4	441598	S3 NOT HAMSTER
5	1404	S4 AND (MUCUS OR MUCOUS)
6	584	S5 AND HUMAN

7	538	S6 AND PY=1993:2013
8	447	S7 AND (EVALUAT? OR ANALYSIS OR TEST? OR VITRO)
9	268	S8 AND (PENETRAT? OR COMPUTER?)
10	134	RD S9 (unique items)

* ITEMS = number of citations retrieved that contain search terms

Sample Titles Retrieved

Single sperm cryopreservation on cryoloops: an alternative to hamster zona for freezing individual spermatozoa. Keywords: cryopreservation methods, semen preservation, spermatozoa physiology, humans, in vitro.

Studies on the development of diluents for the transportation and storage of human semen at ambient temperature. Keywords: environmental temperature, sperm preservation, acrosome reaction, egg yolk, female, hamster, human, spermatozoon motility, penetration.

Computer-Aided Sperm Analysis (CASA) of sperm motility and hyperactivation. Keywords: phase contrast, microscope optics, sperm movement, migration, mucus-penetrating characteristics.

A survey on the status of semen analysis in 118 laboratories in China. Keywords: clinical laboratory techniques, standards, data collection, semen analysis, methods, sperm count, motility.

In this case, consultation with an expert and review of the literature supported information available on refinement, reduction and replacement alternatives. Examples of some of the questions the IACUC may want to ask in the review process may include the following: If hamster oocytes must be used what methods are being used to superovulate and flush oocytes from the hamster? How are the hamsters anesthetized during procedures? What are the fewest number of animals that can be used?

General Comments

Protocols should be evaluated on a case by case basis. A perfect strategy to retrieve every citation regarding reduction, refinement, and replacement does not exist. Many factors may affect the outcome of a literature search, including the area of research, species involved, procedures used, chemical(s) tested, experimental design, and whether or not articles have been indexed. Additional factors include: 1) the degree of communication between the information specialist and the investigator, 2) the knowledge and educational background of the information specialist, and 3) time and money constraints.

References

1. Russell, W. and R. Burch (1959) *The Principles of Humane Experimental Technique* Methuen and Company, London.
2. Stokes, W.S. and D.J.B. Jensen (1995). Guidelines for Institutional Animal Care and Use Committees: consideration of alternatives. *Contemporary Topics* 34(3):51-60.
3. Swanson, J. (March 1991) *Animal Welfare Information Center Scope Notes*. AWIC Series #6. 8 p.

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