Search for Alternatives

A step-by-step approach to an alternatives search

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With special thanks to the Animal Welfare Information Center (AWIC) and the Netherlands Centre for Alternatives to Animal Use (NCA) websites, among others.

Detailed Information on Searching and Databases

Worksheet Essentials (PDF format)

This worksheet is designed to assist researchers with their literature searches, while facilitating compliance with regulatory agencies. The search should identify any alternatives to potentially painful or distressful procedures, while also assuring that the protocol does not unnecessarily duplicate previous research.

The US Animal Welfare Act (AWA) regulations (specifically the 1985 Amendment), require the principal investigators to consider alternatives to procedures that may cause more than momentary or slight pain or distress to the animals, and provide a written narrative of the methods used and sources consulted to determine the availability of alternatives, including refinements, reductions, and replacements.

The search for alternatives refers to the three Rs described in the book, The Principles of Humane Experimental Technique (1959) by Russell and Burch. The 3Rs are reduction in the number of animals used, refinement of techniques and procedures to reduce pain or distress, and replacement of animals with non-animal techniques or use of less-sentient species.

3Rs:

Refinement: The use of analgesics and anesthetics, the use of remote telemetry to increase the quality and quantity of data gathered, and humane endpoints for the animals are examples of refinements.

Reduction: The use of shared control groups, preliminary screening in non-animal systems, innovative statistical packages or a consultation with a statistician are examples of reduction alternatives.

Replacement: Alternatives such as in vitro, cell culture, tissue culture, models, simulations, etc. are examples of replacement. This is also where you might look for any non-mammalian animal models—fish or invertebrates, for example—that would still give you the data you need.
Before you begin your search:

- Consider other possible animal or non-animal models (e.g., tissue culture, cell culture, fish, rats, etc.) (info)
- Consider your objectives and endpoints (info)
- Note any drugs or compounds used in procedures, (e.g., anesthetics, analgesics, test compounds, etc.) (info)
- Note methods and procedures using animals, paying particular attention to those procedures that may cause pain or distress to the animal. (info)
- List any potential alternatives (all 3 Rs) of which you are aware. (e.g., alternate models, modified techniques, housing modifications, modified restraint, in vitro methods, computer simulations, etc.) (info)
- Develop a conceptual search strategy using the keywords and concepts you noted above. A search strategy is necessarily flexible, dependent both on the topic and on the database selected. If too many records are retrieved, additional relevant terms may make the results fewer and more useful; if too little is retrieved, fewer terms and a more conceptual approach may identify the relevant material. Use these terms and concepts as needed when searching in the following databases. (info)
- Database selection: Choose those that are appropriate for the area of study, keeping in mind type of protocol: Is the proposed study a research, teaching, or testing protocol? (info)

For Your protocol

- Note names of databases searched and years covered by the search. (example: PubMed, 1966-2005) (info)
- Note the date(s) on which you searched.
- Describe what alternatives-related information you found, how you are integrating those alternative methods, procedures, or models into your protocol, as well as why you are not using others. This is sometimes referred to as the "narrative" or "search results" section. (info)

Worksheet Guide and Information

This worksheet is a tool used to 1) familiarize the principal investigator with the procedure; 2) identify keywords and concepts that are important in the development of a search strategy; and 3) aid in the selection of appropriate topical databases or other on-line resources. Although this worksheet will help, it is not designed as a replacement for communication between information providers, investigators, veterinarians, and IACUC members.

Searching for possible implementation of reduction and refinement to the study is essential. The use of analgesics and analgesia, the use of remote telemetry to increase the quality and quantity of data gathered, and humane endpoints for the animals are examples of refinements. Use of shared control groups, preliminary screening in non-animal systems, innovative statistical packages, or a consultation with a statistician are examples of reduction alternatives.

Because reduction and refinement aspects of alternatives are broad and often are addressed in the methods section of studies, the search at this point is really a comprehensive look at the field of study. Keywords and concepts from the area of research are used. This in turn addresses whether the protocol unnecessarily duplicates prior research. This approach will result in a basic understanding of the research area, including the literature published in the particular field, the techniques used, and the
commonly used species.

Models: Considering replacement requires that you address potential alternatives such as cell culture, tissue culture, models, simulations, etc. This is also where you might look for non-mammalian animal model—fish or invertebrates, for example—that would still give you the data you need. In addition considering non-animal and alternative animal—models, the proposed animal species should also be searched.

Objectives and Endpoints: As often required for the protocol, write up a complete description of the proposed use of animals, including a succinct outline of the scientific plan and direction of the experiment. When doing a keyword search, the database system searches for words that appear in the title, abstract, and descriptor fields of the citation. Because the painful part of the procedure may be described in the materials and methods sections, the search should focus on the experimental endpoint or objective, in most cases. Exceptions are when methodology papers are common in the field of study (i.e., skin irritation tests, antibody production). Human endpoints, such as indicators of pain, or euthanasia can be searched to determine when the animal should be removed from the study. While endpoints are not easily searchable, they are worth considering when reviewing the search results.

Drugs or compounds: List specific names of drugs you may be using for your study or as anaesthetics or analgesics. (i.e., halothane, rompun, buprenorphine, etc.). Remember to include the scientific and generic name of the drugs. If you are using other compounds in your study, included them when you search the literature for drugs that may conflict or have contraindications with your area of study.

Methods and procedures: Providing the methods and procedures used in your animal study protocol will assist in addressing issues of refinement alternatives, such as handling techniques, restraint techniques, injection techniques, surgical procedures, etc. Identify any painful procedures, along with drugs or methods that will be used to relieve the pain. The law defines a painful procedure as one that would "reasonably be expected to cause more than slight or momentary pain or distress in a human being to which that procedure was applied." If a procedure involves pain or distress, the PI must search for an alternative and, also, consult with the attending veterinarian.

Potential alternatives: Listing terms to describe any potential alternatives you are aware of, such as in vitro, tissue culture, alternative procedures or alternative animal models, etc. is helpful in conducting the refinement alternative aspect of the search. It is also helpful in determining potential search terms to use, since these are terms outside the specific area of study.

Search Strategy: Keywords, concepts and database selection determine the ultimate search strategy. These keywords are those that will likely be found in the title, abstract, and descriptor fields of the citation. Use as many synonyms as possible, such as "cardiac" and "heart." Include acronyms and complete spellings (i.e., "GH" and "growth hormone"). Also include all possible spellings of words. For example, "anesthesia," "anaesthetic," and "anaesthesia." Include words that make the study different from other studies. This will help detect unintentional duplication as well as limit the scope of the search if the number of citations from a broader search is more than 200. All potential alternatives should be included as keywords, whether or not the researcher believes they will be useful. Using the keywords selected from your notes, put together brief strings of words so that each search set covers a separate concept. For example, the first set might include words relating to the experimental outcome, and the second set will contain words relating to the animal model. Short and simple search sentences are preferred. Considering reduction and refinement requires a search similar to the typical literature review done in preparation for a new project or scientific publication. Keywords used will help determine if there is unintentional duplication, how many animals are necessary using the proposed model, appropriate anaesthetics and analgesics, and any other method of minimizing pain and distress. Since much of the refinement and reduction information will be found in the materials and methods sections, it is important for the researcher...
to review some of the articles that may be of interest.

Many people make the mistake of putting the term "alternatives" in the strategy and expect to find all possible alternatives. Because alternatives is a complex concept involving refinement, reduction and replacement, this term is best used only in those areas of study where larger amounts of research have been conducted on alternatives, such as in toxicology or education. They might also end up with "alternatives" that have nothing to do with the 3Rs.

Considering replacement requires a search that should include keywords for potential alternatives such as "vitro," "culture," or "simulation." The word "alternative" may also be included here. The selected animal model, other species, and the word "model" will help retrieve animal and non-animal models as potential alternatives.

Search strategies for research, teaching, or testing protocols differ. For example, a teaching protocol might include keywords such as "teach," "educate," or "instruct," while a testing protocol could include "safety," "efficacy," or "test."

**NOTE:** It is very important to realize that stringing together keywords on one line (i.e., dogs or cats and cardiac or thoracic and stent or device and alternative) does not create a proper search strategy and results in a poor search with inaccurate results. Boolean operators and individual database vagaries require familiarity or professional librarian assistance.

Database selection: The worksheet lists many of the most useful databases for biomedical research topics. Although there is some overlap in journals and other publications covered by the databases, each database is unique; each indexes a unique set of informational resources. Several of the core databases should be searched in order to conduct a comprehensive literature search. Keep in mind the type of protocol when choosing databases. An education protocol, for example, should include ERIC; a protocol involving testing toxic effects of compounds should include TOXNET and RTECS. There are many other specific databases available online – both free and subscription based.

Years of coverage: When a database is chosen on CD-ROM, the World Wide Web, or on a multi-database system, the publication years covered are listed near the title of the database. The searcher should record the years included in the search based on database coverage or the years selected by the searcher within the search strategy (i.e., 1988-2005).

It is important to become familiar with the informational resources, databases, and services available at your institution in order to most effectively perform an alternatives search. The institution's librarian or information specialist can help with this and should be consulted.

Narrative description: A written narrative is required, one that evaluates the search results and assesses the alternative possibilities. It should support the decisions to both use and to not use available alternatives. Be sure to address refinement and reduction alternatives, not just replacement.