



## Institutional Animal Care and Use Committee (IACUC)

### Guidelines for Literature Searches for Alternatives

Date of IACUC Approval: April 8, 2016

Last Updated: July 20, 2017

---

**I. Purpose:** The Brown University IACUC has adopted the following guideline to help research investigators complete the ‘Literature Search for Alternatives,’ which is required by [Animal Care Policy #12](#) (USDA) and Brown’s Animal Welfare Assurance with OLAW, for all Category D (relieved pain/distress) or E (unrelieved pain/distress) procedures for USDA-regulated species and/or Department of Defense funded protocols.

**II. USDA Classifications:**

**Classification D:** Animals upon which experiments, teaching, research, surgery, or tests will be conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs will be used.

**Classification E:** Animals upon which teaching, experiments, research, surgery, or tests will be conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs will adversely affect the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests.

**III. Background:**

The literature search must include more than one database search. Conferences, consultants and search engines (i.e., Google Scholar) may also be used, *in addition* to a minimum of two different databases. Consultants include statisticians and subject matter experts. For non-database sources, please supply the consultant’s name, qualifications, and the date and content of the consult.

The purpose of the literature search is to look for ways to incorporate the “3 Rs” into an animal use protocol:

- **Replacement:** the study uses a non-animal model or a species deemed to be lower on the phylogenetic scale (e.g., *in vitro* culture instead of an animal or a mouse model instead of a dog).
- **Refinement:** the study has minimized animal pain and distress. This includes using the least painful technique, using appropriate anesthesia and analgesia, and incorporating humane endpoints.

- **Reduction:** the study uses the minimum number of animals necessary to accomplish experimental objectives. Statistical tests (e.g., power analysis) should be used to confirm that the minimum number of animals is requested for the protocol.

Consider contacting a Brown University librarian to assist in the search. A more comprehensive [Alternative Search Guide](#) was developed in partnership between the University Library and the IACUC to aid researchers performing literature searches for animal alternatives. Other useful tools include the Animal Welfare Information Center (AWIC), the UC-Davis [Center for Animal Alternatives](#), [Altweb](#) at Johns Hopkins, [Altbib](#) and the references specifically cited elsewhere in this document.

#### IV. **Procedure:** Step-by-step process to perform an acceptable literature search for alternatives:

1. Develop a comprehensive list of keywords.
  - a. Consider non-animal models that may be available, such as computer simulations or *in vitro* cultures. Potential search terms include “alternative,” “simulation,” “model” and “in vitro.”
  - b. Consider the potential application of phylogenetically lower animal models, such as fish or invertebrates. Justify why they cannot be used for the proposed studies.
  - c. Add keyword search terms pertaining to the specific research objectives, any procedures listed as Category D or E, particular techniques, drugs, anesthesia and analgesia, species and strain of animal, and ‘endpoints.’
    - i. Use synonyms, acronyms and alternative spelling to increase the number of search results. The [MeSH](#) function in Pubmed will help find the medical subject heading and any subheadings, allow restriction or explosion of the heading, and help build searches.
    - ii. Use of the terms “severity” or “assessment” in the search string may help find refinements or humane endpoints.
  - d. A search of each painful or distressful (category D or E) procedure should include at least one of the following appropriate search terms: “refine” or “refinement,” “analgesia,” “alternative,” “pain,” “distress,” “humane endpoints.”
2. Combine keywords into brief search strings.
  - a. Keep strings brief to maximize search results or ‘hits.’
    - i. For example: when considering search strings for refinements (non-painful or less painful alternatives to painful/distressful procedures) to a mouse cecal ligation and puncture procedure one might include:
      - cecal ligation and puncture model pain severity
      - cecal ligation and puncture animal pain assessment
      - cecal ligation and puncture analgesia

- ii. Further examples of search strings looking for replacement and reduction (alternatives to the species used) could include:
      - peritonitis simulation
      - septic peritonitis in vitro
      - peritonitis sample size
      - ("Peritonitis"[MeSH]) AND ("Animal Use Alternatives"[MeSH])
      - peritonitis AND ("birds" OR "reptiles" OR "amphibians" OR "fish")
    - b. If searches resultant in excessive 'hits,' consider adding or combining terms to help narrow the search.
    - c. Develop separate search strings for each potentially painful/distressful procedure.
  3. Select databases based on your research area. Commonly used databases include [PubMed](#), [Biological Abstracts](#), [PsychInfo](#), [Agricola](#), [Web of Science](#), [TOXNET](#), [Scopus](#), and [BIOSIS](#). Some laboratory animal and welfare focused journals and magazines can also be useful resources: [Altex](#), [Lab Animal](#), [JAALAS](#), [JAAWS](#). Search engines may also be used as a resource (i.e., Google Scholar), but a minimum of two different databases is required.
  4. Search the strings in the databases. Be sure to record the database, search string, date searched, and dates the search covered. Most databases allow you to save searches by creating an account, for example, "My NCBI" in PubMed.
  5. Review any relevant papers that you find; 'Materials and methods' sections of papers are especially important to review for alternatives.
  6. Determine whether you can incorporate any of your search findings into your research plan and related IACUC protocol application.
  7. Briefly describe your search and its outcome; this should be done in a narrative format (e.g., paragraph). If no relevant information was found, state so.