Search for Alternatives
IACUC Guideline

**Purpose**
Principal investigators must consider alternatives to any procedure likely to produce pain to or distress in experimental animals (AWAR³).

**Scope**
This requirement applies to all species; however, for research involving USDA-covered animals, the methods and sources used must be documented in the IACUC protocol.

**Considerations**
Alternatives should be considered in the planning phase of an animal use proposal as a meaningful search will inform experimental design. This should be performed with consideration the Three Rs²:

- **Replacement**: Address the feasibility of using alternative methods to achieve experimental aims, including in vitro models, in silico methods, invertebrate models, and/or more appropriate vertebrate models.
- **Reduction**: Demonstrate that the proposed studies do not unnecessarily duplicate previous work. Consider reusing animals for other purposes. Incorporate statistical methods to reduce animal numbers.
- **Refinement**: Consider methods that may minimize or eliminate pain and/or distress to improve animal welfare.

Investigators must assess any potential alternative possibility and justify why it cannot be incorporated into the experimental design.

**Documentation**
Investigators should perform a search for alternatives using two or more sources. One source must from a relevant database such as PubMed. The search must be documented with the name of the database, search terms, date of search, and time period covered for every applicable species and procedure.

An appropriate consultation can be used as a secondary source. The consultation must be documented with the consultant's name and qualifications, and date and content of the consult to demonstrate the expert's knowledge of the availability of alternatives in the specific field of study.

**Designing Search for Alternatives**
Use the following questions to guide your search for replacement and reduction alternatives:

- Are there in vitro techniques that may reduce or replace the number of animals used (e.g. chorioallantoic membrane assays, primary cells, cell lines, etc.)?
- Are there lower species or more informative animal models (e.g. invertebrates, fish, microbes, etc.)?
- Are there computer models or simulations that could replace animal use?
- Are there statistical methods that would reduce sample size?
Use the following questions to guide your search for refinement alternatives:

- Are there surgical approaches that are less invasive?
- Are there anesthetics or analgesics that are more effective?
- Are there experimental endpoints that are earlier than those proposed or other ways to shorten post-procedure times?
- Are there other means to lessen the pain or distress of the procedure or improve the welfare of the animal, such as alternative housing or alternative animal identification methods?

Resources

A search for alternatives with regards to the Three Rs is not the same as searching for recent advances in your field of science or medicine. Special search strategies are required to find meaningful results. The resources linked below may provide guidance on how to conduct a proper literature search.

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<th>Resource</th>
<th>Description</th>
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<tr>
<td>Ask a Librarian</td>
<td>Countway librarians at the Harvard Longwood Campus are always available to help with search for alternatives.</td>
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<tr>
<td>Meeting Requirements for Alternatives Searches (OLAW Webinar)</td>
<td>This online seminar covers the role of literature searches in the consideration of alternatives, as well as some strategies and resources that can be helpful when performing literature searches.</td>
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<tr>
<td>MeSH Tutorial (PubMed Online Training)</td>
<td>PubMed uses a specialized vocabulary to structure information, the &quot;Medical Subject Headings&quot; (MeSH Terms). To perform an effective search for alternatives, it is essential that you use MeSH Terms; relevant results may not be found otherwise. MeSH Terms are specific words and phrases drawn from the National Library of Medicine's controlled vocabulary. Use the MeSH Terms Browser to find the MeSH Terms most appropriate for your study.</td>
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<td>Tip</td>
<td>The [MAJR] qualifier identifies a MeSH Term which is a main topic of the article. Use [MAJR] in place of [MeSH] and [ALL] to find the subset of articles focused on the search terms. Compare the &quot;focused&quot; and &quot;inclusive&quot; examples below to see the effect of using the [MAJR] qualifier.</td>
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<td>Alternatives Literature Searching (Animal Welfare Information Center)</td>
<td>AWIC offers expertise in the formulation of search strategies and the selection of terminology and databases, and on- and off-site training of institute personnel in conducting effective alternatives searches.</td>
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<td>Worksheet: Alternative Literature Searching &amp; Tips for Searching for Alternatives to Animal Research and Testing (AWIC)</td>
<td>These are designed to assist researchers when conducting literature searches to determine if alternatives exist and whether the protocol unnecessarily duplicates previous research.</td>
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<td>National Centre for the Replacement, Refinement, &amp; Reduction of Animals in Research</td>
<td>The NC3Rs is a UK-based scientific organization that provides an extensive library of 3Rs resources.</td>
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References

1. Animal Welfare Act and Regulations (AWAR) [7 USC, § 2143(a)(3)(B)].