

**Subject:** Consideration of Alternatives to Painful/Distressful Procedures **Policy #12**

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**References:** AWA Section 2143(a)(3)(B)  
9 CFR, Part 2, Section 2.31 (d)(1)(ii)and (e); Section 2.32 (c)(2) and (5)(ii)  
Principles of Humane Experimental Techniques, William Russell and Rex Burch, 1959  
Public Health Service Policy on Humane Care and Use of Laboratory Animals (IV,C,5)  
Animal Welfare Information Center

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**History:** Replaces policies dated April 14, 1997, and June 21, 2000.

**Justification:** The Animal Welfare Act (AWA) regulations require 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.

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**Policy:** Alternatives or alternative methods, as first described by Russell and Burch in 1959, are generally regarded as those that incorporate some aspect of replacement, reduction, or refinement of animal use in pursuit of the minimization of animal pain and distress consistent with the goals of the research. These include methods that use non-animal systems or less sentient animal species to partially or fully replace animals (for example, the use of an in vitro or insect model to replace a mammalian model), methods that reduce the number of animals to the minimum required to obtain scientifically valid data, and methods that refine animal use by lessening or eliminating pain or distress and, thereby, enhancing animal well-being (for example, the use of appropriate anesthetic drugs). However, methods that do not allow the attainment of the goals of the research are not, by definition, alternatives.

Alternatives should be considered in the planning phase of the animal use proposal. As indicated when these regulations were finalized in 1989, APHIS continues to recommend a database search as the most effective and efficient method for demonstrating compliance with the requirement to consider alternatives to painful/distressful procedures. However, in some circumstances (as in highly specialized fields of study), conferences, colloquia, subject expert consultants, or other sources may provide relevant and up-to-date information regarding alternatives in lieu of, or in addition to, a database search. Sufficient documentation, such as the consultant's name and qualifications and the date and content of the consult, should be provided to the IACUC to demonstrate the expert's knowledge of the availability of

alternatives in the specific field of study. For example, an immunologist cited as a subject expert may or may not possess expertise concerning alternatives to *in vivo* antibody production.

When a database search is the primary means of meeting this requirement, the narrative should include:

1. the name(s) of the databases searched (due to the variation in subject coverage and sources used, one database is seldom adequate);
2. the date the search was performed;
3. the time period covered by the search; and
4. the search strategy (including scientifically relevant terminology) used.

The Animal Welfare Information Center (AWIC) is an information service of the National Agricultural Library specifically established to provide information about alternatives. AWIC offers expertise in formulation of the search strategy and selection of terminology and databases, access to unique databases, on- and off-site training of institute personnel in conducting effective alternatives searches, and is able to perform no-cost or low-cost electronic database searches. AWIC can be contacted at (301) 504-6212, via E-mail at [awic@nal.usda.gov](mailto:awic@nal.usda.gov), or via its web site at <http://www.awic.nal.usda.gov>. Other excellent resources for assistance with alternative searches are available and may be equally acceptable.

Regardless of the alternatives sources(s) used, the written narrative should include adequate information for the IACUC to assess that a reasonable and good faith effort was made to determine the availability of alternatives or alternative methods. If a database search or other source identifies a bona fide alternative method (one that could be used to accomplish the goals of the animal use proposal), the IACUC may and should ask the PI to explain why an alternative that had been found was not used. The IACUC, in fact, can withhold approval of the study proposal if the Committee is not satisfied with the procedures the PI plans to use in his study.

The rationale for federally-mandated animal testing (for example, testing product safety/efficacy/potency) should include a citation of the appropriate government agency's regulation and guidance documents. Mandating agency guidelines should be consulted since they may provide alternatives (for example, refinements such as humane endpoints or replacements such as the Murine Local Lymph Node Assay) that are not included in the Code of Federal Regulations. If a mandating agency-accepted alternative is not used, the IACUC must review the proposal to determine adequate rationales have been provided, and pain and discomfort limited to that which is unavoidable.

Significant changes are subject to prior review by the IACUC. If those changes include a painful or distressful procedure, a consideration of alternatives or a revision of the prior search may be required

Although additional attempts to identify alternatives or alternative methods are not required by Animal Care at the time of each annual review of an animal protocol, Animal Care would normally expect the principal investigator to reconsider alternatives at least once every 3 years, consistent with the triennial *de novo* review requirements of the Public Health Service Policy on Humane Care and Use of Laboratory Animals (IV,C,5).