



Remote Production of Custom Antibodies

372.1 Policy: The purchase of custom polyclonal and monoclonal antibodies requires the submission and approval of an animal use protocol through the Institutional Animal Care and Use Committee (IACUC).

In deferring the majority of the protocol review to the contracted production agency, the IACUC retains responsibility to obtain documentation indicating the activity was reviewed and approved by the IACUC of the contracted producer and that the contracted producer is a registered facility with the USDA and possesses a valid PHS Assurance. In instances where investigators are using vertebrate animals in their research endeavor and must submit an animal use protocol for IACUC review and approval, this can be accomplished in the TOPAZ Web P&R protocol system simply as an amendment.

If the investigator is contracting for outside custom-made antibodies, there are no sections in the TOPAZ Web P&R protocol system to specifically collect the necessary additional information such as (PHS Assurance, USDA license number, IACUC information at the contracted site, etc.). In instances where the investigator's research does not require the use of vertebrate animals except for the production of antibodies, abbreviated procedures to obtain IACUC approval will be used to request IACUC review and approval. In addition, the mandatory educational requirements are waived for the principal investigator and the research staff as no live animals are handled or manipulated directly by the Emory research personnel in these instances.

In reviewing an application for contracted polyclonal or monoclonal antibody production the Emory IACUC office shall verify that the contracted agency or firm has a valid PHS assurance and, if a covered species is involved, that the agency or firm is registered with the United States Department of Agriculture as a Research Facility. A copy of the contracted agency or firm's IACUC protocol approval and date of approval shall be included in the TOPAZ Web P&R protocol system protocol file as attachments.

The Emory University IACUC retains a responsibility to ensure that the contracted production is scientifically justified, minimizes pain and distress to the animals involved, and is not duplicative. A complete copy of the polyclonal or monoclonal antibody protocol being used by the contracted agency or firm, including details concerning adjuvants used, the injection protocol, and analgesics used will be submitted and attached to the TOPAZ Web P&R protocol system protocol file. If these items have been reviewed and approved by the remote production facility, the IACUC Office can issue approval. The investigator must make a good faith effort to identify and use commercially available antibodies potentially suitable for the proposed work. The use of on-line antibody search engines (<http://www.abcam.com/>) should be an integral component of the search for "duplication." The databases searched, the date of the search, and the results will be required entries on the future "IACUC Protocol Application:

Custom-made Antibodies” form. If antibodies are commercially available and the research requires custom-made antibodies, scientific justification must be provided as to why the commercially available antibodies were deemed unacceptable.

If the ascites method of monoclonal antibody production is to be used, sufficient information must be provided to the IACUC to “determine that (i) the proposed use is scientifically justified, (ii) methods that avoid or minimize discomfort, distress, and pain (including in vitro methods) have been considered, and (iii) the latter have been found unsuitable.” (OPRR REPORTS, Number 98-01, November 17, 1997).

The purchase of commercially available polyclonal or monoclonal antibodies does not require the submission of an animal use protocol or approval of the Institutional Animal Care and Use Committee (IACUC). Commercially available antibodies are those already produced and available usually through company catalogs or antibody suppliers such as Abcam (<http://www.abcam.com/>).

372.2 Definitions of Key Terms Specific to this Policy: Custom polyclonal and monoclonal antibodies are those produced either from antigen provided by the contracting investigator or through the generation of a specific polypeptide that is then used to immunize animals to produce antibodies.

372.3 Applicability: This policy applies to all Emory research related activities that fall under the IACUC’s jurisdiction.

372.4 Background: The Public Health Service first clarified this requirement in 1995 in an OPRR REPORTS (Number 95-02, Animal Welfare, March 8, 1995) distributed to all PHS-funded institutions (<http://grants.nih.gov/grants/olaw/references/dc95-3.htm>);

“A common example of this is the production of antibodies using antigens provided by an investigator ("custom" antibodies) in animals. Institutions and investigators should be aware that if animals are utilized to produce such antibodies for use in PHS-supported research, the organization producing those antibodies must either have on file with OPRR (now OLAW) an approved Animal Welfare Assurance (Assurance) or be included as a component of the applicant organization's Assurance. In addition, if species covered by the Animal Welfare Act are utilized, the producer must be registered as a "Research Facility" with the U.S. Department of Agriculture (USDA).”

The Public Health Service requirements were further clarified in 2001 with the release of a Notice in the Federal Register (NOT-OD-01-017, February 12, 2001) [<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-01-017.html>];

“If both institutions have full PHS Assurances, they may exercise discretion in determining which IACUC reviews research protocols and under which institutional program the research

will be performed. It is recommended that if an IACUC defers protocol review to another IACUC, then documentation of the review should be maintained by both committees. Similarly, an IACUC would want to know about any significant questions or issues raised during a semiannual program inspection by another IACUC of a facility housing a research activity for which that IACUC bears some responsibility or exposure.”

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NOTICE: NOT-OD-01-

017

Update: The following update relating to this announcement has been issued:

[March 18, 2011](#) - See Notice NOT-OD-11-053 Guidance to Reduce Regulatory Burden for IACUC Administration Regarding Alternate Members and Approval Dates.

[July 14, 2010](#) - See Notice NOT-OD-10-114 Update on Applicability of the Shelf Life Extension Program (SLEP).

National Institutes of Health

This notice provides guidance to Public Health Service (PHS) awardee institutions and Institutional Animal Care and Use Committees (IACUCs) concerning the following two administrative IACUC issues: use of alternate IACUC members and IACUC protocol and programmatic review at collaborating institutions. It further provides an example of an existing drug shelf life extension program that may be utilized to extend the expiration date of certain pharmaceuticals in an animal care and use program. A renewed Memorandum of Understanding (MOU) among USDA, FDA and NIH is also announced.

BACKGROUND

The Office of Laboratory Animal Welfare (OLAW), NIH, and the USDA Animal and Plant Health Inspection Service have continued to work with the NIH Advisory Working Group on Regulatory Burden established in January, 2000, to assist and advise the NIH on issues and recommendations presented in the report "NIH Initiative to Reduce Regulatory Burden." As a result of ongoing discussions about administrative issues dealing with the ways that IACUCs function and efforts by IACUCs to conduct business more efficiently, OLAW is issuing the following guidance. The purpose of the guidance is to ensure that IACUCs policies and procedures are in accordance with the PHS Policy on Humane Care and Use of Laboratory Animals and, as applicable, the USDA animal welfare regulations (AWRs). The USDA Animal and Plant Health Inspection Service (APHIS) has reviewed and concurs with the guidance provided in this notice.

USE OF ALTERNATE IACUC MEMBERS

Although PHS Policy and the USDA AWRs are silent on the use of alternate IACUC members, OLAW and APHIS agree that alternates may be utilized if the following provisions are met:

- o Alternates must be appointed by the chief executive officer (CEO) of the entity for which the committee is established, or by the official to whom the CEO has specifically delegated, in writing, authority to appoint IACUC members. Alternates should be listed on the IACUC rosters submitted to OLAW with Assurances and annual reports.
- o There must be a specific one-to-one designation of IACUC members and alternates. This is necessary to ensure that a committee is properly constituted, even when alternates are serving. For example, an alternate for a non-affiliated IACUC member would need

to also meet the non-affiliated member requirements. Use of a pool of alternates would not be consistent with this requirement.

- o An IACUC member and his/her alternate may not contribute to a quorum at the same time or act in an official IACUC member capacity at the same time. An alternate may only contribute to a quorum and function as an IACUC member if the regular member for whom they serve as alternate is unavailable.

- o Alternates should receive IACUC training or orientation similar or identical to what is provided regular IACUC members.

- o Alternate members would be expected to "vote their conscience" as opposed to representing the position of the regular member for whom they serve.

- o Alternate members may be permitted to attend IACUC meetings and participate in other IACUC activities even when the regular member is present, at the discretion of the institution, although as stated above they may not contribute to the formation of a quorum or vote unless the member for whom they substitute is not available.

NO REQUIREMENT FOR DUPLICATE REVIEW

There are many circumstances that involve partnerships between collaborating institutions or relationships between institutional animal care programs. OLAW and APHIS agree that review of a research project or evaluation of a program or facility by more than one recognized IACUC is not a federal requirement.

It is imperative that institutions define their respective responsibilities. PHS Policy requires that all awardees and performance sites hold an approved Animal Welfare Assurance. OLAW negotiates Interinstitutional Agreement Assurances of Compliance when an awardee institution without an animal care and use program or IACUC will rely on the program of an Assured institution. Assured institutions also have the option to amend their Assurance to cover nonassured performance sites, which effectively subjugates the performance site to the Assured institution and makes the Assured institution responsible for the performance site.

If both institutions have full PHS Assurances, they may exercise discretion in determining which IACUC reviews research protocols and under which institutional program the research will be performed. It is recommended that if an IACUC defers protocol review to another IACUC, then documentation of the review should be maintained by both committees. Similarly, an IACUC would want to know about any significant questions or issues raised during a semiannual program inspection by another IACUC of a facility housing a research activity for which that IACUC bears some responsibility or exposure.

DOD SHELF LIFE EXTENSION PROGRAM (SLEP)

The Department of Defense Shelf Life Extension Program (SLEP), on the internet at <http://www.jrcab.army.mil/fda/page1.html>, was developed to defer drug replacement costs of date sensitive military reserve stock by extending the useful life of pharmaceutical products. The program involves the identification of candidate items by DOD Service representatives to a Joint Readiness Clinical Advisory Board, which submits products to the FDA. The FDA requires submission of samples and evaluates candidate materials using original manufacturer's test data to establish a protocol for testing. The testing conducted by the FDA is comprehensive and

scientifically sound, and FDA bases expiration date extensions on conservative estimates of the useful life of the product as substantiated by the test results. specified by lot number, expiration date, and manufacturer that have been stored under appropriate conditions.

The FDA grants the extensions as

Institutional animal care and use programs, although ineligible to submit candidates for testing, may access the database of items tested and expiration date extensions. Identified pharmaceutical products (specified by lot number) used in animal care and use programs that have new expiration dates need not be replaced until after the new expiration date. Both OLAW and USDA will recognize the validity of the new expiration dates assigned through the SLEP program.

MEMORANDUM OF UNDERSTANDING

In January, 2001, USDA, FDA and NIH renewed a Memorandum of Understanding (MOU) Concerning Laboratory Animal Welfare. Since 1995 the three agencies have operated under an MOU that provides for enhanced communication and allows common concerns of the agencies to be managed in a consistent and coherent manner in spite of differing statutory or regulatory mandates. The MOU is perhaps most effective in serving to ensure that the differing approaches of the agencies are harmonized without unnecessarily increasing regulatory burden. Renewal of the MOU signals a willingness to continue the long-standing cooperation that has been of mutual benefit to the agencies while fostering proper animal care and welfare. The new MOU is posted at:
<http://grants.nih.gov/grants/olaw/references/finalmou.htm>.

INQUIRIES

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