Procedure for Addressing PHS Animal Protocol-Proposal Congruency Requirements at the UMass Medical School

Section I. Introduction

A. In recent years, the NIH Office of Laboratory Animal Welfare has increasingly emphasized the importance of NIH-funded institutions proactively ensuring that their Investigators comply with all Animal Welfare regulations. Through a series of statements, the most recent in November 2013, OLAW has made it clear that in order to retain their right to receive NIH funding, institutional research compliance officials must verify that all vertebrate animal research activities have been reviewed prior to award acceptance to ensure congruence between the protocol and the grant proposal.

These requirements may be confusing to investigators who have been accustomed to greater latitude in previous years or at previous institutions. However, in order to safeguard the entire faculty, the institution must set and follow the currently accepted standards for congruency review.

The procedure described below is intended to help investigators by removing any ambiguities about the process and defining review parameters in order to fulfill NIH congruency requirements necessary for the release of your grant funds.

Section II. Background

A. NIH Grants Policy Statement (GPS)

[Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General, Section 4.1.1.2: Verification of IACUC Approval](#) reads:

"NIH will delay an award for research involving live vertebrate animals until the grantee organization and all performance sites are operating in accordance with approved Animal Welfare Assurances and the grantee has provided verification of Institutional Animal Care and Use Committee (IACUC) approval of those sections of the application that involve use of vertebrate animals. IACUC approval must have been granted within three years of the budget period start date to be valid; however, IACUCs may determine that continuing review on a more frequent basis is appropriate.

Verification of IACUC approval may be filed at any time before award in accord with Just-in-Time (JIT) procedures, unless required earlier by the Institutes and Centers. Therefore, following peer review and notification of impact score/percentile, applicant organizations with approved Assurances may wish to proceed with IACUC review for those applications that have not yet received IACUC approval and that appear to be in a fundable range.

It is an institutional responsibility to ensure that the research described in the application is congruent with any corresponding protocols approved by the IACUC.

No costs for activities with live vertebrate animals may be charged to NIH grants if there is not a valid IACUC approval."

It is important to recognize that compliance with the PHS Congruency Policy is a term and condition of the GPS. The GPS defines contractual or legal obligations between UMMS and NIH. If UMMS accepts PHS funds and fails to meet the terms and conditions, there can be fiscal, civil, and/or criminal penalties.

B. Definition of Congruency Review

A congruency review is a side by side comparison of a proposal (grant, award, contract, subaward, etc.) to a protocol to ensure that the animal activity outlined in the grant

proposal has been approved by the UMMS IACUC and is reasonably similar to the activity contained in an approved animal protocol. A congruency review is required for all PHS funding that uses live vertebrate animals to ensure that the work described in the proposal comports with an active, approved protocol. UMMS has a one-to-many/many-to-one system which means a funded proposal can be linked to one or many protocols, and one protocol can be linked to one or many proposals.

Section III. Scope and UMMS Procedure

Most NIH applications with a live animal vertebrate research component are submitted with a pending IACUC status. Most Principal Investigators (PIs) will not prepare and submit an IACUC protocol until they have an indication that the application may be funded.

NIH uses a JIT approach to information that they request after an application has been peer reviewed and is within a range of possible funding. Receiving a just-in-time request does not guarantee or indicate in any way whether an applicant will get an award.
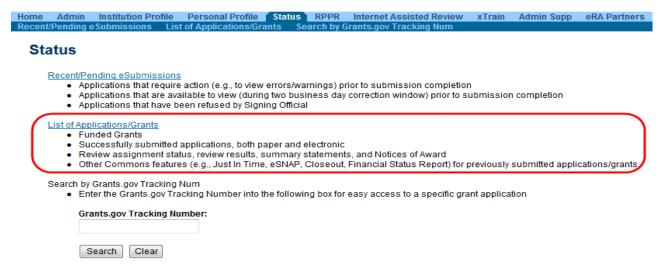
Information required after peer review includes a number of compliance requirements including verification of IACUC approval.

NIH will send an automated email request for JIT information within 15 days after releasing the score for all applications with overall impact scores of 40 or less.

It is at this initial automated request (referred to in this document as JIT Stage 1) that the Office of Sponsored Programs (OSP) will reach out to PIs via email and ask them to address the grant protocol congruency requirement if they have what they consider to be a fundable score. Investigators will be directed to retrieve their e-Application in eRA Commons and include it as an attachment to their email. Please *"reply all"* when responding so that all parties remain copied when requesting the congruency review. The PI is also requested to include all protocol numbers related to the project in this email as well.

RETRIEVING THE E-APPLICATION FROM eRA COMMONS

To retrieve your e-Application, log into eRA Commons then Click on *Status* on the selection bar:

The Status screen will appear. Click on the List of Applications/Grants:

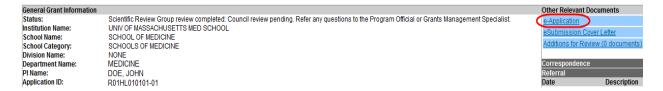# Procedure for Addressing PHS Animal Protocol-Proposal Congruency Requirements at the UMass Medical School

The screen below will appear. Depending on your application history, you may have to sort through multiple applications to select the appropriate project. Once, identified, click on the *Application ID* on the left.

Status Result - General Search ❓

>>If your grant was not awarded, please do not use the MYPR link in the Action column to submit a Progress Report for Mult-Year Grant.<<

Tips and Notes:

- PD/PI column shows Contact PI for multi-PI grants.

Application ID	Grants.gov Tracking #	Proposal Title	PD/PI Name	Application Status	Budget Start Date
1R01HL010101-01	GRANT12345678	Test Proposal	DOE, JOHN	Pending Council Review	04/01/2014

This will open the *Status Info* screen. On the right, under the section labeled *Other Relevant Documents*, you will find your e-Application:

Status Information

General Grant Information		Other Relevant Documents
Status:	Scientific Review Group review completed: Council review pending. Refer any questions to the Program Official or Grants Management Specialist.	e-Application
Institution Name:	UNIV OF MASSACHUSETTS MED SCHOOL	eSubmission Cover Letter
School Name:	SCHOOL OF MEDICINE	Additions for Review (0 documents)
School Category:	SCHOOLS OF MEDICINE	
Division Name:	NONE	
Department Name:	MEDICINE	Correspondence
PI Name:	DOE, JOHN	Referral
Application ID:	R01HL010101-01	Date Description

Click on the *e-Application* to open the pdf.   This is the document that needs to be submitted for congruency review should your application be close to the fundable range.

Beyond JIT Stage 1, NIH Grant Staff will submit individual ad hoc requests to PIs and OSP for additional JIT information not submitted previously or to request updated other support and/or compliance assurances (referred to in this document as JIT Stage 2). A JIT Stage 2 request is usually a strong indicator an award will be funded.

For proposals with a live animal vertebrate research component, OSP will verify whether the congruency review was completed at JIT Stage 1. If not, OSP will provide a copy of the e-Application to the congruency reviewer and the Investigator via email and ask the Investigator to provide an approved protocol number or initiate the IACUC protocol application process.

Please be aware that JIT Stage 2 turnaround times are usually short and may not allow sufficient time for a congruency review to be conducted. If this occurs, OSP will submit the JIT Stage 2 response with the IACUC approval listed as pending.

Section IV. Congruency Review

A. Congruency review will be performed on a first-come first-serve basis by an Office of Research designated reviewer with expertise in and familiarity with regulations for conducting vertebrate animal research. Investigators should allow for at least one week for completion of the review. The congruency review is not automatic and will only be performed at JIT Stage 1 at the request of the PI and at JIT Stage 2 at the request of OSP if it has not been previously reviewed/addressed.

B. At JIT Stage 1, <u>the PI</u> will provide the following information to the congruency reviewer:

Procedure for Addressing PHS Animal Protocol-Proposal Congruency Requirements at the UMass Medical School

1. A copy of the agency reviewed *e-Application* downloaded from eRA Commons (any other version is not acceptable).

2. The docket numbers of applicable IACUC approved protocols.

At JIT Stage 2, OSP will provide the following information to the congruency reviewer via email (with copy to PI):

1. A copy of the agency reviewed *e-Application* downloaded from eRA Commons.

2. The docket numbers of any previously disclosed protocols related to the application.

C. The reviewer will verify congruence between the grant proposal and corresponding IACUC approved protocol(s) in the following specific areas. The congruency reviewer may request more information or clarification from the PI during the review.

1. General scope of the work (disease area, target organs, biological targets, etc.)

2. Species (including strain(s), if the conduct of the proposed study or the disease model is dependent on the strain)

3. Approximate numbers of animals

4. Experimental procedures and endpoints

5. Agents (experimental and therapeutic)

6. Euthanasia method

> A reasonable matching description of the above areas in the grant proposal and IACUC-approved protocol will be regarded as congruence. In general, reviews that require minor amendments (excluding off-site protocols) will be deemed to be congruent as well as major amendments not impacting the elements of review listed above.

Note: If there are live animal studies conducted by external collaborator(s) or service providers (e.g., antibody production), an off-site protocol is required for UMMS IACUC review. All external collaborators or vendors must have IACUC approvals from NIH-assured entities and should be listed in the UMMS animal study protocol in Form J or in a stand-alone off-site protocol.

Section V. After congruency review

A. The PI and OSP will be notified by the reviewer of the outcome of the congruency evaluation. The PI will have an opportunity to clarify issues and/or provide additional relevant information to achieve congruence.

B. **If congruent**, UMMS will submit the JIT response without any pending items for the proposed study. Please note that congruency does not mean full agreement between your grant proposal and IACUC protocol(s).

C. **If non-congruent**, The PI will receive notification from the reviewer (with copy to OSP) along with a description of the discrepancies and suggestions on how the discrepancies can be resolved. If the PI disagrees with the reviewer's determination, they are advised to contact the reviewer to discuss the matter and provide additional documentation in support

of their position. If these discussions result in a determination of congruence, no further action will be required by the PI.

If non-congruent, PIs will need to amend their IACUC protocol or submit a new protocol to address the incongruity if there are clear discrepancies between the grant proposal and IACUC protocol(s) in any of the 6 areas identified in Section III.C. Such modifications need to be processed and approved by the IACUC *via* the standard protocol review and approval mechanisms, prior to certifying grant-protocol congruency.

Section VI. Tips for PIs to avoid delays in accepting funds due to non-congruency:

PIs are advised to take the following steps after the submission of a research proposal (grant, award, contract, subaward, etc.) to facilitate timely congruency review.

1. If you receive a high priority score, OSP recommends consulting with your Program Officer to see whether you are within funding range. When you learn that your grant application is potentially fundable, please conduct a review of your IACUC protocol(s) to confirm that all the studies in the proposal are included in an IACUC-approved protocol. The self-review should focus on the six areas identified in Section IV.C.

2. If all proposed studies are not included in the IACUC protocol, modify the IACUC protocol, or submit a new protocol or early renewal, if necessary. Please plan ahead as IACUC requires about 3-4 weeks to approve a major amendment, or 4-8 weeks to approve a new protocols or renewal.

3. If the current protocol is set to expire before or within a few months of the award start date, it is advisable to submit a new protocol or an early renewal of the IACUC protocol.

4. A detailed description is not required for studies planned for <u>years 4 and 5</u> of the grant or for <u>alternative approaches</u> to be taken if the planned studies are not successful. For this exception to the congruency requirement, OLAW/NIH has advised a brief description of such studies in lieu of a detailed experimental design in the IACUC protocol is acceptable. A detailed description of these studies with IACUC approval will be required prior to initiating them by amending or renewing the IACUC protocol.

5. **Studies conducted at outside or off-site institutions**. The UMMS PI should ensure that non-UMMS collaborators planning to conduct off-site live animal studies (via contract/subaward), or producing not off the shelf research reagents (e.g., antibody production) provide their approved IACUC protocol to the UMMS IACUC for review and approval. NIH requires that all external collaborators must have IACUC approvals from NIH assured entities. UMMS investigators must complete an off-site protocol form or amend their approved protocol by completing Form J.

Section VII: Common Congruency Review Questions

Is it acceptable for institutions to ask each PI to confirm that all animal work described in the grant has been approved by the IACUC?

OLAW/NIH discourages this practice as it places the institutions at significant risk, and some of the institutions who have used this practice have been required to return funds to NIH for non-compliance.

Procedure for Addressing PHS Animal Protocol-Proposal Congruency Requirements at the UMass Medical School

Why can't the study section review of the Vertebrate Animal Section fulfill the requirement for congruency review?

Scientific review group (SRG) or study section is not intended to supersede or serve as a replacement for IACUC. SRG only verifies that the proposed use of animals is scientifically appropriate, whereas IACUC approval indicates that the protocol has been determined to confirm to the PHS policy.

Is it better to have one IACUC protocol for each grant?

NIH indicates that this is for the institution to decide. UMMS has a one-to-many/many-to-one system which means one funded proposal can be linked to one or many protocols, and one protocol can be linked to one or many proposals. UMMS has tended to encourage protocols that approve animal use in more than one grant unless the sponsor specifically requires its own dedicated protocol.

Is congruency with an IACUC-approved protocol necessary for the alternative methods?

Yes, but the details provided may be less for the alternative procedures if the PI states in the IACUC protocol that the protocol will be amended if the original plans are changed.

Since the grants are typically approved for 5 years and the protocols are approved for 3 years, are the PIs required to include in the IACUC protocol experiments proposed to be performed in the 4th and 5th years?

Years 1 to 3: During the congruency review, the IACUC-approved protocol is expected to contain details of experiments to be conducted in the first 3 years of the grant application. If the current IACUC-approved protocol is close to its expiration date, it is advisable to submit a new protocol instead of modifying the current protocol prior to the congruency review.

Years 4 and 5: The 4th and 5th year experiments in the grant application should be briefly described in the IACUC protocol with the explanation that details will be added at a later time, typically at the end of the 3-year cycle of the IACUC protocol prior to initiating the studies.

Does the institution need to do a congruency review for external collaborators or service providers?

Animal use studies can be only performed at PHS assured institutions/providers with an IACUC protocol covering the studies requested by the UMMS investigator. The external collaborators can submit a congruency verification or information to UMMS. Information may include a copy of approval protocol, a copy of approval letter and their PHS Assurance number, and UMMS investigators can include information about off-site animal studies in their IACUC protocols.