

Ethical Review of Research with Animals and Humans: Congruence and Administrative Requirements for Studies with Multiple Sites

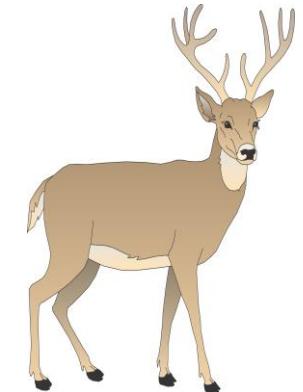
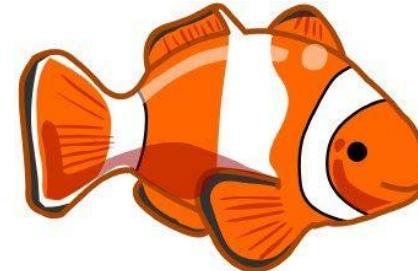
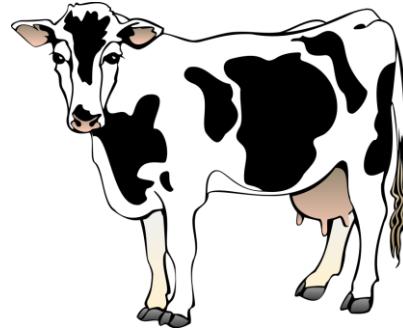
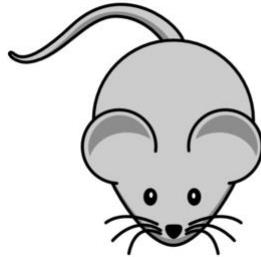
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Overview of key administrative requirements
as they apply to the IACUC (animal subjects)
and IRB (human subjects) oversight, including
those pertaining to collaborative research
with more than one institution

Requirements for Congruence, MOUs, and Inter-Institutional Assurances for Animal Studies



Goals

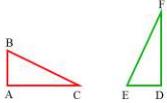
Explain the requirements for achieving grant and protocol congruence for an animal study performed at UD or for a subaward to another institution.

Review when memorandums of understanding MOUs or inter-institutional assurances should be established.



The Idea of a Congruence

Two geometric figures with exactly the same size and shape.



Congruence

Congruence is agreement between the animal activities described in a grant and the animal activities reviewed and approved by the IACUC.



Why is Congruence a requirement?

NIH Grants Policy Statement (NIHGPS)

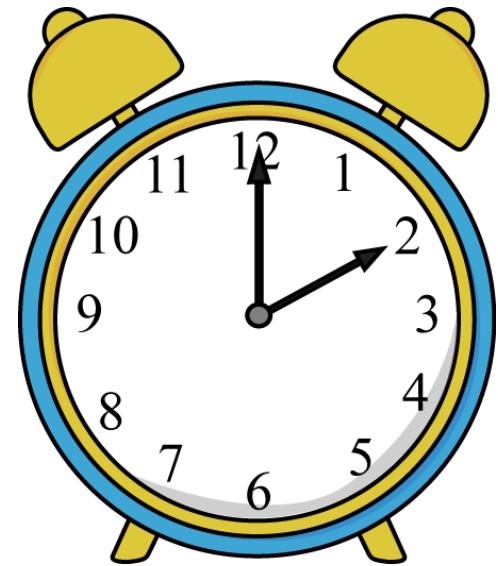
“It is an institutional responsibility to ensure that the research described in the application is **congruent** with any corresponding protocols approved by the IACUC.”

NIHGPS Part II, A, 4.1.1.2 Verification of IACUC Approval



When May Congruence Be Determined?

Any time **prior** to grant award.



Who May Review for Congruence?

Someone who is qualified to identify inconsistencies and has access to the IACUC protocol and grant application, e.g., :

IACUC staff

Sponsored projects staff

Compliance oversight personnel



Who is Responsible?

Institution verifies congruence by providing IACUC approval date

Institution (via the AOR) and **PI** are responsible for notifying NIH of a change in scope or IACUC required modifications

PI must notify IACUC of change in scope as a result of NIH review

PI is responsible for obtaining IACUC approval of proposed animal activities



What About Other Agencies?

Department of Veterans Affairs

National Science Foundation

Department of Defense

USDA National Institute of Food and Agriculture



Where to Look in the Grant

Vertebrate Animals Section
Research Strategy Section



What Content Should Be Compared?

Species

Total animal numbers proposed

Procedures



Issues That May Require Clarification

- Animal numbers
- Performance site
- Administration of agents
- Change in species

Change in scope?



Indicators of Change in Scope

- Change in the specific aims approved at the time of award
- Substitution of one animal model for another
- Change from the approved use of live vertebrate animals
- Shift of the research emphasis from one disease area to another

NIHGPS Part II: Subpart A: 8.1.2.5 Change in Scope



Does the IACUC Protocol Match the Grant?

Is it documented?

Institutions should maintain **congruence review records** for their own purposes and have them available for possible review by NIH.

There are numerous ways to achieve and verify congruence.

Institutions may develop and implement their own policies and procedures, as long as those policies and procedures satisfy the requirements of the PHS Policy and the terms and conditions of NIH Grants Policy.

Congruence Review Strategy Summary

- Concentrate on Vertebrate Animals Section
In Research Strategy, focus on Approach
- Look for key words describing procedures in
the IACUC protocol and in the grant
- If inconsistent, have PI clarify and provide
explanation
- If PI changes protocol or grant, notify NIH if
grant is impacted





If two institutions are involved in a project, which one is responsible to ensure congruence?

The institution that receives NIH funds or the institution that has an IACUC and provides animal care?

Answer: The institution that receives NIH funds



When institutions collaborate, or when the performance site is not the awardee institution, which IACUC is responsible for review of the research activity?

There are many circumstances that involve partnerships between collaborating institutions or relationships between institutional animal care programs. Interinstitutional collaborations have the potential to create ambiguities. Therefore it is imperative that institutions define their respective responsibilities. 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. Institutions should have a formal written understanding (e.g., memorandum of understanding) that addresses responsibilities for animal care and use, ownership, and IACUC review and oversight (*Guide page 15*) .

Memorandum of Understanding (MOU):

-Used when the subrecipient will be conducting vertebrate animal federally-funded research under its own assurance

Inter-Institutional Assurance (IIA):

-Used when one party to a collaboration will be conducting vertebrate animal research under the other party's assurance



MOU – both entities (PTE and subawardee) have an IACUC assurance. Animals are being used at the subsite. Both institutors have an assurance, but only one needs an IACUC approval. Place where the work is being conducted is primarily responsible for the requirements.

Inter-Institutional Assurance (IIA) – specific to the OLAW office – subawardee does not have their own IACUC program (example may be a drug company), and therefore the site contracts with another institution that has their own IACUC program. The IIA is issued by OLAW and must be in place before grant funds are released to the subsite. The IIA is only good for the life of that grant.



RESEARCH INVOLVING HUMAN SUBJECTS



Research with Human Subjects:

A **systematic investigation** to develop or contribute to generalizable knowledge that involves: (1) obtaining **information or biospecimens through intervention or interaction** with living individuals; or (2) obtaining, using, studying, or analyzing, or generating, **identifiable private information or identifiable biospecimens**.



- Federalwide Assurance (FWA)
- Required IRB approval of each study
 - Changes in scope requiring prior approval
- Reliance Agreements
- Single IRB
- Data Use Agreements





FederalWide Assurance (FWA)

- A Federal Wide Assurance (**FWA**) is the documentation of an institution's commitment to comply with Federal regulations and maintain policies and procedures for the protection of human participants.
- An institution must have an FWA in order to receive federal support/funding for research involving human subjects.
 - Must be renewed every 5 years
- UD applies the requirements of its FWA to all research involving human subjects research regardless of funding source

FWA and SUBS:

- When UD is prime of a federally funded study involving human subjects research and subbing some of that work to another institution **we must ensure the sub also holds an active and current FWA**
 - If collaborator in a UD-led study is a **single investigator/small practice** that does not hold an **FWA protections can be extended via an Individual Investigator Agreement (IIA)**
 - The **UD IRB office** will assist on that determination and **processing of the agreement**



IRB APPROVAL REQUIREMENTS:

- “Certification is required when the research is supported by a federal department or agency and not otherwise waived under 45 CFR 46.101(i) or exempted under 45 CFR 46.104. For such research, institutions must certify that each proposed research study covered by the assurance and 45 CFR 46.103 has been reviewed and approved by the IRB. Such certification must be submitted as prescribed by the federal department or agency component supporting the research. Under no condition shall research covered by 45 CFR 46.103 be initiated prior to receipt of the certification that the research has been reviewed and approved by the IRB.” (45 CFR 46.103(d)).”

Institution is responsible for certifications when accepting awards

IRB APPROVAL FOR EACH STUDY

- IRB reviewed study(ies) must match and include the funded award
 - **IRB review and approval must be obtained prior to release of funding**
 - **JIT:** Just in Time, agencies (NIH) normally accept for review and approval to be sought after PI has been notified of likelihood of funding.
- **More than one IRB approval per award:** A single award may contain several studies within, all studies must be reviewed and approved
 - PI is responsible for ensuring all proposed work is reviewed and approved by the IRB
 - IRB approval letters must list study title and PI name.
 - They may or may not have expiration date



CHANGE IN SCOPE

- **PIs are responsible for submitting for IRB review and approval any amendment to previously approved research prior to its implementation**
- **NIH: If the changes could result in an increased risk they may require prior NIH approval:**
 - From non-human subjects to human subjects (exempt or non-exempt)
 - From exempt to non-exempt
 - From no clinical trial to clinical trial
 - Inclusion of new subject populations (e.g., children, prisoners, pregnant women)
 - Changes that could increase the overall risk of the study



RELIANCE AGREEMENTS (IAAs)

- Institutions have the option of relying on another institution's IRB review, approval, and oversight of a study in which they are engaged.
- Institutional Authorization Agreement (IAA) is the documentation of that reliance.
 - Normally IAAs are agreed upon and signed on a study-by-study basis
- Reliance decisions are made by the IRB Office
- In order for UD to rely on another Institution's IRB review that institution must have an active FWA





UD IRB REVIEW

- The **UD IRB must be informed by the UD investigator of all studies in which they are engaged** in human subjects research (even if led by another PI/Institution)
 - All studies with UD researchers must be submitted to the UD IRB **via IRBNet**
- The **UD IRB only provides review and oversight of studies that include a UD investigator.**
 - Decisions about reliance or multiple IRB review are made by the IRB Office depending on the specifics about the study and the involved sites



SINGLE IRB REVIEW

- NIH expects that all sites participating in multi-site studies, which involve non-exempt human subjects **research funded by the NIH**, will use a **single Institutional Review Board (sIRB) to conduct the ethical review required for the protection of human subjects** (for applications after January 25, 2018)
- A **reliance is required** – **UD IRB Office must be informed ASAP**
- **Investigators must comply with several sets of requirements**, their own institution requirements and those of the reviewing IRB
- **SMART IRB: National IRB Reliance Initiative**



DATA USE AGREEMENTS (DUA)

- Terms for the **proper sharing of data** (normally sensitive) **between institutions**
- **DUAs are not required by the rules the IRB oversees** but often associated with data from human subjects research
 - Commonly used in the exchange of protected health information (PHI)
- **DUAs requirements vary from institution to institution**
- Often signed at the institutional level

