DF/HCC

DANA-FARBER / HARVARD CANCER CENTER

BIOSPECIMEN RESEARCH: UNTANGLING MYTHS, TRUTHS, REGULATIONS, CONTRACTS AND AGREEMENTS

BIOSPECIMEN RESEARCH:
UNTANGLING MYTHS, TRUTHS, REGULATIONS, CONTRACTS AND AGREEMENTS

Agenda

- **Introductions & Background**
- **IRB Overview & Review Requirements**
- **Patient Samples and Agreements**
- **Grants & Funding**
- **Q & A**

Speakers

Jeffrey Meyerhardt, MD, MPH- Moderator

Deputy Clinical Research Officer, DFCI

IRB D Co-Chair, DF/HCC

Emily Eldh, CIP

Director, DF/HCC Office for Human Research Studies (OHRS)

Mary Melloni, RN, JD, MBA

Director, DFCI Clinical Research Agreements Office

Anita Ballesteros, PhD

Senior Licensing Associate, Belfer Office for Dana-Farber Innovations (BODFI)

Tina Da Silva, CRA

Director, DFCI Grants and Contracts

DF/HCC

DANA-FARBER / HARVARD CANCER CENTER

IRB Overview & Review Requirements

Emily Eldh

Director, Office for Human Research Studies

IRB Overview & Review Requirements

- **Defining Secondary Use Research**
- **IRB Review Requirements**
- **Case Studies**
- **OHRS Tools**
- **Changes to Regulatory Requirements**
- **References and Resources**

DF/HCC

DANA-FARBER / HARVARD CANCER CENTER

Defining Secondary Use Research

The Common Rule

- The **Common Rule** is a 1981 **rule** of ethics in the United States that governs research involving human subjects.
  - The rule requires Institutional Review Board (IRB) oversight of human subjects research
  - Baseline standard of ethics by which 18 federal agencies have agreed to follow for government-funded research
  - Nearly all U.S. academic institutions (including DFCI) hold their researchers to these regulations regardless of funding
  - The common rule is encapsulated in the 1991 revision to the U.S. Department of Health and Human Services **Title 45 CFR 46** (Public Welfare) Subparts A, B, C and D.
  - FDA is not a signatory to the Common Rule.

Regulatory Definition of Research

- **Systematic investigation**, including research development, testing and evaluation, designed **to develop or contribute to generalizable knowledge.**

45 CFR 46.102 Definitions

Regulatory Definition of a Human Subject

A living individual about whom an investigator (whether professional or student) conducting research obtains:

1. **Data through intervention or interaction with the individual**

OR

2. **Identifiable private information (ie. PHI)**

45 CFR 46.102 Definitions

What is Secondary Use Research?

Research on data and/or specimens that were **previously collected for another purpose** (research or clinical purposes)

- Existing data must include "**private information**" in order to constitute research involving human subjects

  For example:

  - Review of medical records, data collected from previous studies, audio/video recordings, or images, etc.

DF/HCC

DANA-FARBER / HARVARD CANCER CENTER

Secondary Use Research – IRB Review Requirements

Secondary Use IRB Review Requirements

- Projects using secondary use data, such as an **existing data set** which includes identifiable, private data **gathered in earlier research projects (including banking protocols)** may require a new IRB protocol for review ***IF***
  - Specimens are **identifiable**
  - Specimens are coded and researchers receiving the specimens may **readily ascertain** the identity of the individual from whom the specimens were obtained
  - Specimens are de-identified but the study is testing a drug or device and results will be **submitted or held for review by the FDA** *(uncommon)*

How do Banking Protocols work?

Banking protocols generally do not propose <u>specific</u> research, but create:

- a repository or database;
- with specific parameters for future use;
- and a plan for data or repository governance *(e.g. Honest Broker, User committee).*

Honest Broker

What is an Honest Broker?

- An honest broker is a person or system that acts as a neutral intermediary between the individual (PHI) whose tissue and data are being studied and the researcher (deidentified).
- The honest broker collects and collates pertinent information regarding the tissue source, replaces identifiers with a code, and **releases the sample with only coded information to the researcher**.

User Committees

What is a User Committee?

- Reviews the feasibility and scientific validity of proposed clinical research, QI projects, translational and laboratory-based projects[1] that propose the use of clinical data and/or biospecimens previously collected for research purposes
- Reviews both Human Subjects Research and Non-Human Subject Research
- However, **User committee review does not replace IRB review**. Human Subjects Research must also be reviewed by the IRB.

1. DF/HCC Breast Users Committee and Resources for Research web page. http://www.dfhcc.harvard.edu/research/research-programs/clinical-based-programs/breast-cancer/program-resources/dfhcc-breast-users-committee/

IRB Review Requirements

Sharing and Future Use:

- Banking protocol consent forms must include a plan for sharing and future use of specimens
- The IRB is responsible for the review of subsequent studies proposing to use data and/or specimens from a banking protocol.
- IRBs may not delegate their authority for review of these secondary use submissions
- IRBs must consider the original consent form to determine if the proposed research aligns what was initially described to participants

Current IRB Review Requirements

Sharing and Future Use:

A New IRB submission (or amendment) may be required if an investigator receives:

- Identifiable private information (PHI) linked to specimens;
- Identifiers included in the data set; or
- Data or specimens that the study team can identify.

A New IRB submission <u>may not</u> be required if:

- All samples/data are completely de-identified (or coded) with an agreement (MTA/DUA) that investigators will not reidentify individual subjects.

Example:

Consider if Investigator Smith is listed on the banking protocol and then requests “de-identified” or “coded” specimens from that bank. Investigator Smith, by nature of being listed on the original banking protocol has access to identifiers and/or the code linked to identifiers and could readily ascertain the identity of individual subjects.

Current IRB Review Requirements

IRB Review Determinations:

Expedited Category 5 *(Typical)*

Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis)

- **Required submissions**
  - New Project Application – Non-Clinical Research and all requested supplemental materials
  - Amendments
  - Continuing Reviews
  - Unanticipated events
  - Privacy board review

Current IRB Review Requirements

IRB Review Determinations:

Exempt Category 4

(Rare and Not applicable to FDA-regulated research)

- Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
- **Required submissions**
  - New Project Application – Non-Clinical Research and all requested supplemental materials
  - Protocol
  - Amendments
  - Unanticipated events
  - Privacy Board review

Current IRB Review Requirements

Full Board Review *(Less Likely)*

- Greater than minimal risk
- Not exempt category 4 or expedited category 5

- **Required Submissions**
  - New Project Application and a Protocol
  - Consent Form (which may be waived/altered)
  - Amendments
  - Continuing Reviews
  - Unanticipated Events / Deviations / Adverse Events
  - Privacy Board Review

Current IRB Requirements:

Waivers of Informed Consent or Authorization (Minimal Risk & Practicability)

HHS & FDA 45 CFR 46.116(d) and FDA Guidance issued 07/25/2017

- No more than minimal risk
- Waiver would not adversely affect the rights and welfare of subjects
- Research could not practicably be carried out without the waiver
- Subjects will be provided with pertinent information after participation, whenever appropriate

HIPAA Authorization can be waived by the IRB/Privacy Board if

- Use or disclosure involves no more than minimal risk to the individual's privacy
- Research could not practicably be conducted without the waiver
- Could not practicably be conducted without use or disclosure of the protected health information

DF/HCC

DANA-FARBER / HARVARD CANCER CENTER

Secondary Use Research– Case Studies

Case Study #1 – Dr. Shah:

Tissue biopsies were obtained for clinical diagnostic purposes, which have now been satisfied. The patients did not provide study specific informed consent for the research use of the tissue specimens. The hospital pathology department is willing to provide a portion of the remaining biopsy specimens to Dr. Shah who will perform research assays. In order to allow matching with relevant clinical information, the specimens will be provided with identifiers such that the investigator can readily ascertain the identity of subjects.

Is consent of the patient from whom the biopsy was taken (or waiver of consent) required for the secondary research use?

Case Study #1 - Response

- **HHS Common Rule Issues**
  - **Yes, Informed consent should either be obtained or waived** under 45 CFR 46.116(d) because the samples are identifiable to the recipient investigator
  - An IRB approved research protocol must also cover the research.
- **HIPAA Issues**
  - **Patient HIPAA Authorization** or a **IRB/Privacy Board Waiver of Authorization** is required because this involves use or disclosure of patient identifiers for the research purpose
- **FDA Required IRB review** - Uncommon
  - Only if the tissues are used to test an **FDA regulated IVD**
  - Participant informed consent must be obtained

Case Study #1 – Dr. Shah's Next Steps:

HHS Common Rule Issues

- Submit a New Protocol Application (NPA) for Non-Clinical Research including:
  - Data and Specimen Collection Protocol Template
  - Any other supplemental materials outlined in the NPA checklist
  - The study team may request a waiver of informed consent (or draft a consent document).

HIPAA Issues

- Request a waiver of HIPAA Authorization. The waiver request and justification for the waiver should be described in the protocol template.

FDA Issues - uncommon

- Only required If the tissues are used to test an FDA regulated IVD, OHRS will help identify if FDA applies
- Required New protocol and IRB review
- Informed consent is required

Case Study #2 – Dr. Kronish:

Tissue biopsies were obtained for clinical diagnostic purposes, which have now been satisfied. The hospital pathology department is willing to provide Dr. Kronish a portion of the remaining biopsy specimens to an investigator who will perform research assays. The specimens will be coded such that the investigator will not be able to readily ascertain the identity of individuals

Is consent of the patient from whom the biopsy was taken (or waiver of consent) required for the secondary research use?

Case Study #2 - Response

- **HHS Common Rule Issues**
  - None. De-identified samples do not fall into the definition of human subjects. Neither consent nor a waiver is required.
- **HIPAA Issues**
  - None. Specimens that are de-identified in accordance with HIPAA do not contain PHI. Neither authorization nor an IRB or Privacy Board waiver of the authorization or review is required.
- **FDA Issues** - uncommon
  - Only if the tissues are used to test an FDA regulated IVD
  - IRB review is required
  - Consent may or may not be required. See the FDA "Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable"

Case Study #2 – Dr. Kronish's next steps:

- **HHS Common Rule**
  - Submit a request for a Not Human Subjects Research Determination.
  - A determination from OHRS is typically required to satisfy funding agency requirements.

- **FDA** - Uncommon
  - Submit the New Protocol Application (NPA) for Non-Clinical Research along with the Data and Specimen Collection Protocol Template and other required materials as outlined in the NPA Checklist.

Case Study #3 – Dr. Long:

Blood samples were obtained for research purposes, with informed consent of the subjects, and the original study has been completed. The samples remain under the control of the original investigator. Dr. Long wants to use a portion of the remaining samples to perform research completely unrelated to the original study.

If the original consent stated that "…your sample will only be used for research on colon cancer," but the secondary user is interested in studying Alzheimer's disease, can the samples still be used if provided to the secondary user in a coded fashion?

Case Study #3 - Response

- **HHS Common Rule Issues**
  - The secondary use of de-identified or coded samples is not research involving human subjects under 45 CFR 46.
  - In the case where secondary use of tissue samples is not compatible with the original consent for tissues that are de-identified, coded, or anonymized and are not readily identifiable, the samples are no longer subject to human subject regulations.
  - There is no regulatory violation if the coded samples are used for the non-cancer research; **however, the original investigator and his/her institution have made an agreement with the subjects about use of their specimens, and have an obligation to honor that agreement.**

Case Study #3 – Response (cont'd)

- **HIPAA Issues** - PHI
  - If there was a need to disclosure direct identifiers for the new research purpose, it would require a study-specific HIPAA authorization from the subject; or an IRB or Privacy Board waiver of the authorization requirement.
  - If the research could be performed using only information about the subject that constitutes a limited data set, the original investigator could disclose the limited data set to the researcher after the researcher has signed a data use agreement (DUA) that complies with the requirements in 45 CFR 164.514(e)(4).

- **FDA Issues** - Uncommon
  - If tissues are used to test an FDA regulated IVD, then IRB review is required.
  - It may not be necessary to obtain informed consent of the subjects for the secondary use if the seven conditions are met in the FDA "Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable."
  - FDA agrees with the considerations described above regarding the ethical obligation to the subjects.

Case Study #3 – Dr. Long's Next Steps:

- **HHS**
  - If required, submit a Request for Not Human Subjects Research (NHSR) Determination and identify all studies from which data/samples are requested.
  - A NHSR determination is typically required to satisfy funding agencies
  - If original collection did not occur at DF/HCC sites, the releasing institution is responsible for reviewing consent forms to ensure that data/samples are used in accordance with the terms of the original consent.
- **FDA** - Uncommon
  - Submit a New Protocol Application for Non-Clinical Research along with a completed Data/Specimen Collection Protocol template.
    - Identify all studies from which data/samples are requested

Case Study #4 – Dr. Durie:

Patients undergoing surgery provide Dr. Durie informed consent to donate any excess tissue (i.e., beyond that needed for clinical purposes) to a DF/HCC tissue bank. The creation of the DF/HCC tissue bank is reviewed and approved by the DFCI IRB. The consent form makes it clear that the specimens and associated clinical data will be used for research, but does not specify or limit that use.

If specimens are provided to the researchers with clinical information that allows the researcher to readily ascertain the identity of the subjects, do those DF/HCC researchers need separate IRB approval of the proposed research use of the specimens and data?

Case Study #4 - Response

- **HHS Common Rule Issues**
  - Yes, the provision of identifiable information with the specimen(s) means the research to be conducted with the specimen is a separate human subjects research protocol and separate IRB approval would be required.
  - In general, banking protocols describe only the potential future use for data/specimens maintained in the database or repository
  - IRB review of research is required when identifiable private information is released from the bank or repository or investigators are able to readily ascertain the identity of individuals from whom samples or data were obtained.

- **FDA Issues** - Uncommon
  - If the tissues are used to test an FDA regulated IVD, then separate IRB review is required.

Case Study #4 – IRB Review Requirements and Next Steps:

IRB Submission Requirements:

- **New Protocol**
  - Submit a new protocol describing the use of banked data and/or specimens including specific research aim(s)
  - Include all Investigators and Sponsors
- **Amend the Banking Protocol***
  - Add individual specific projects to the banking protocol, including specific research aims
  - Add all Investigators to the overall banking protocol study team
  - Add all Sponsors to the banking protocol

**The Overall PI of the banking protocol is responsible for all research added as a sub-study.*

DF/HCC

DANA-FARBER / HARVARD CANCER CENTER

Future Changes to Regulatory Requirements

Changes to Regulatory Requirements

- 7/19/2018 – Revised HHS Regulations (delayed from 1/19/18)
  - Changes include (but not limited to):
    - Reorganization of consent to included new Key Information section
    - New required elements of consent regarding future use of Data and Samples
    - Removes continuing review requirements (for certain “minimal risk” studies)
    - Expands Exempt review categories (this means even fewer studies requiring annual continuing review)
    - Introduces new concept of “Limited IRB Review” for Exempt Research

Changes to Regulatory Requirements, continued

- 1/25/2018 - NIH Single IRB Policy
  - All NIH-funded non-exempt multi-center research must now be reviewed by ONE IRB
  - NIH Clinical Trial Definition: https://grants.nih.gov/policy/clinical-trials/definition.htm

- 1/20/2020 – HHS Single IRB Review Requirements
  - All Federally-funded studies must be reviewed by ONE IRB

DF/HCC

DANA-FARBER / HARVARD CANCER CENTER

Secondary Use Research – Tools and Resources

OHRS Tools to Assist with Submission Preparation & IRB Review

- **OHRS Webpage on Research with Data and Biological Materials**

  http://www.dfhcc.harvard.edu/research/clinical-research-support/office-for-human-research-studies/research-with-biological-materials-data/

- **Protocol Template – Data/Specimen Collection and/or Use**
- **New Protocol Application – Non-Clinical Research**
- **Application – Not Human Subjects Research Determination**
- **Review Guidance (Info Sheet)**
- **Secondary Use Research Guidance (Info Sheet)**
- **Worksheet – Human Research Determination**

External Resources

- SACHRP Guidance: FAQs, Terms and Recommendations on Informed Consent and Research Use of Biospecimens (2011)

  https://www.hhs.gov/ohrp/sachrp-committee/recommendations/2011-october-13-letter-attachment-d/index.html#

- Partners Human Research Committee Guidance: Human Tissues: Brief Primer on Research Use and Requirement for Partners IRB Review

  https://partnershealthcare-public.sharepoint.com/ClinicalResearch/TissuePrimer.pdf

- University of California Irvine IRB FAQs – "Does secondary analysis of a data set gathered for another purpose require a new research project for review?"

  http://www.research.uci.edu/compliance/human-research-protections/researchers/irb-faqs.html#Does

- NCCN Points to Consider on the Best Practices for Biorepositories, Registries and Databases

  https://www.nccn.org/clinical_trials/RepositoriesBestPractices.aspx

OHRS Resources

- DFCI IRB Requirements Relating to the Honest Broker in Biobanking

  http://www.dfhcc.harvard.edu/crs-resources/OHRS_Documents/02_-_Investigator_Resources/IS_-_Policy_-_DFCI_IRB_Requirements_Relating_to_the_Honest_Broker_in_Biobanking.pdf

- DFCI Policy – NIH Updated Genomic Data Sharing Policy

  http://www.dfhcc.harvard.edu/crs-resources/OHRS_Documents/02_-_Investigator_Resources/IS_-_Policy_-_NIH_Updated_Genomic_Data-Sharing_Policy.pdf

- DFCI Policy – Linked and Anonymous Specimens

  http://www.dfhcc.harvard.edu/crs-resources/OHRS_Documents/02_-_Investigator_Resources/IS_-_Policy_-_Linked_and_Anonymous.pdf

- DFCI Policy – Collecting and Sharing Data and Tissue Specimens

  http://www.dfhcc.harvard.edu/crs-resources/OHRS_Documents/02_-_Investigator_Resources/IS_-_Policy_-_Collecting_-_Sharing_Data_and_Tissue_Specimens.pdf

DF/HCC

DANA-FARBER / HARVARD CANCER CENTER

Patient Samples and Agreements

Mary Melloni,

Director, Clinical Research Agreements

Anita Ballesteros,

Senior Licensing Associate, Belfer Office for Dana-Farber Innovations

Offices Involved in Research Agreements

Services provided by offices

Clinical trials Agreements Office

- Agreements for lab analysis under a clincial trial protocol:
  - Lab Services Agreement
  - MTA to Broad for trial sample sequencing as part of trial
  - Data Transfer or Data Use Agreement to share trial data

Belfer Office of Dana-Farber Innovations (BODFI)

- Agreements to cover research that is *not* part of a clinical trial, including but not limited to: MTAs, research collaborations, DTAs/DUAs, sponsored research.

Sharing Samples Outside the Institution

- ANY time a patient sample or specimen or data is transferred from the Institution there must be a paper trail in place that tracks the samples:
  - Written in a DFCI IRB Protocol (for clinical trial samples) AND/OR
  - Separate agreements such as:
    - Material Transfer Agreement (MTA)
    - Lab Services Agreement
    - Data Transfer Agreement (DTA)
    - Collaboration Agreement

Sharing Samples Outside the Institution

- Any Institution outside of DFCI qualifies as an external institution and an MTA or DTA is required.
- This includes the Broad, BWH, BCH, MGH, BIDMC.
- For clinical trials with a DF/HCC protocol, no additional transfer agreement is required ***if*** the transfer has been approved in the protocol and all parties participating in the protocol are parties under a Clinical Trial Agreement ***or*** Subcontract.

Sharing samples outside the Institution

- PI Initiated Clinical trials:
  - For a PI initiated, Industry supported study where samples are being sent out for lab analyses (usually but not always at a cost to DFCI), an agreement (Lab Services Agreement or Research Support Agreement) needs to be established with the outside lab regardless if the lab is a commercial lab or an academic lab.

Sharing samples outside the Institution

- ANY time there is a charge incurred to the Institution for the outside laboratory services for the trial there must be an Agreement in place.
- We should never be invoiced to pay an outside entity for a service without an agreement in place that lists the work to be performed and the cost. Without an agreement Finance cannot pay the invoices.
- The Purchased Services Agreement or Research Services Agreement will describe the tests to be performed, the obligations of the parties, where invoices should go to and the agreed upon cost.

Sharing samples outside the Institution

- For a PI Initiated, Industry supported study and Industry is managing the lab analyses and paying for the analyses, this should be stated in the Protocol and no additional agreements need to be established with the outside lab (Vendor is contracted with by the Company).

Industry's impact on trial samples

Industry sponsored trial samples

- Samples are not transferable
- Use of samples only in accordance with protocol
- No DFCI future research use unless authorized by the Industry Sponsor and the Informed Consent Form

PI Initiated trial samples

- Future research use that may identify the drug in the sample must be discussed with funding company before additional use. Contact CTAO to discuss as may be contractually prohibited.
- Cannot collaborate with another company on sample research unless and until obtain approval from Company who funded trial (IP encumbered on drug and possible restrictions on use)

Clinical Trial Samples to Broad Institute for Analysis

- DFCI has several Master Services Agreements and template Material Transfer Agreement to uses for the various types of research being performed as part of the clinical trial
- **There is no umbrella agreement with the Broad** for research projects involving human samples.
- The Broad Institute is not part of DFCI and thus every time a sample leaves DFCI to be shipped to Broad for analysis an agreement governing the transfer must be put in place.

Broad Institute Lab Analysis (cont'd)

- Please contact the Clinical Trial Agreement Office or your BODFI Case Manager if you have samples from a clinical trial to be analyzed at the Broad (**even at your own Broad Lab**).
- We will discuss what research is being performed (i.e. is it part of the trial or correlative analysis on banked trial samples), whether it is for CLIA-lab genomic sequencing or other research, and identifying the Broad PI and Case Manager.
- This information will help determine what type of agreement is needed and what office (CTAO or BODFI) will handle the agreement.

Past BODFI Practices

- Historical paradigms for sharing patient-derived material with external, for-profit companies:
  - SRA — where samples are kept in-house and DFCI investigators conduct the research
  - MTA / collaboration — where samples or PDX models are sent to the company for free, with the understanding that the company will return data to DFCI and allow our researchers to share authorship in any journal publications of the research results

What We Need to Evaluate Requests

- Investigator info, recipient info, PI sign-off
- Type of patient-derived material
- Methods of patient sample collection
- Types of proposed research relationships
- Language in patient consents
- Whether PI requesting sample transfer vs. PI that is actual "custodian" of samples & IRB protocol
- Proposed economics

- **We have to track information and categorize requests**

DF/HCC

DANA-FARBER / HARVARD CANCER CENTER

DANA-FARBER CANCER INSTITUTE

GRANTS AND CONTRACTS

Office of Research

Grants and Congruency Review

IRB Review of Applications for HHS Support

- Department of Health and Human Services (HHS) regulations at 45 CFR 46.103(f) require that each *application or proposal* for HHS-supported human subject research be reviewed and approved by the Institutional Review Board (IRB). hhs.gov

- Office of Human Subjects Research Protections (OHRP) has identified numerous instances in which human subject research described in an application for HHS support differed significantly from the IRB-approved protocol that was claimed by the investigator to constitute the research in the application. In each case, the application added important elements (e.g., targeting of vulnerable subjects; additional treatment arms; different drug dosages; additional collaborators or performance sites) that were ultimately implemented without IRB review and approval.

IRB Review of Applications for HHS Support

- HHS regulations require that the IRB review the actual application or proposal for HHS support. The IRB's review should ensure that all research described in the application or proposal is entirely consistent with any corresponding protocol(s) submitted to the IRB.

- This review need not be undertaken by every IRB member. Rather, a designated IRB member may document that the proposed research is consistent with any relevant protocol(s) submitted to, or previously approved by, the IRB. A copy of the HHS application or proposal should be retained among IRB records and made available to any IRB member who may wish to review it.

NIH Grants Policy Statement
4.1.15.2 Certification of IRB Approval

- IRB approval must have been granted within 12 months before the budget period start date to be valid. **Note** that NIH requires the date of final IRB approval; conditional IRB approval is not sufficient. *In the case of IRB approval with conditions, IRB approval only becomes effective when the IRB has approved all information submitted in response to their conditions.*

- Certification of IRB approval is generally requested at Just-In-Time (JIT) unless required earlier by the funding institute/center.

- Following peer review and notification of impact score/percentile, investigators should proceed with IRB review for those applications that have not yet received IRB approval and that appear to be in a fundable range **or** request congruency review of previously approved protocol(s). This will reduce award issuance delays.

- https://grants.nih.gov/grants/policy

Award Acceptance

- In accepting an award that supports human subjects research, the grantee institution assumes responsibility
  - for all research conducted under the award, including protection of human subjects at all participating and consortium sites, and
  - for ensuring that a Federal Wide Assurance (FWA) and certification of IRB review and approval exists for each site before human subjects research may begin.
  - The investigators acknowledge and accept responsibility for protecting the rights and welfare of human subjects and for complying with the FWA.

When is Congruency Review Required?

- Congruency review is required for all non-exempt HHS-supported human subjects research.

- Exempt research projects may not require full congruency review; however, proposals need to be checked by the IRB to ensure that exemption is appropriate for the work proposed in the grant application.

- The IRB is responsible for assessing whether the grant proposal/contract and protocol are in alignment.
  - Incongruence requires new protocol or amendment
  - If the comparison identifies significant discrepancies or incongruence, OHRS will work with the Principal Investigator (PI) to amend existing protocol or initiate a new IRB protocol, as appropriate.

- G&C cannot setup the award until those discrepancies have been resolved and OHRS issues an updated approval.

Just-In-Time (JIT) Requests

- At JIT, the NIH Grant Management Specialist (GMS) requests that DFCI provide the IRB approval date.

- For projects with new protocols, that date is the IRB approval date
  - *IRB reviewed the protocol against the grant application*

- For projects that utilize pre-existing protocol(s), the IRB approval date should be the congruency review approval date.
  - *Ensures that IRB has reviewed the grant application against the protocol(s) and determined consistency.*
  - *If Amendment or Continuing Review approval comprised of a review of the protocol against the grant application, that approval qualifies as congruency review*.

Case Study

G&C receives JIT email request from GMS “I have completed my review of the above referenced grant application for possible NCI funding. Please have a business official associated with this award confirm if Dana-Farber Cancer Institute is still interested in accepting this R01 at NCI’s funding level of 91.5%.

Additionally please provide the following information:

- Provide the negotiated indirect cost rate agreement for Dana-Farber
- Provide the IRB approval date
- Provide certification of human subjects education training
- Provide other support documentation for key personnel
- Finally, please confirm if a potential December 1st start date will be acceptable

Please provide the requested information by January 25th. If you need additional time please let me know as soon as possible.

G&C received four (4) Protocol Memos with JIT Materials:

- Two protocols were active
  - Approval dates prior to the submission of the R01 application
  - No reference of congruency review of the R01 application
- One protocol was non-human subject research
  - Determination made in March 2014
  - No reference of congruency review of the R01 application
- One protocol was expired
  - Expiration in October 2015, but Department wanted to include as an IRB memo because it shows the genomic data sharing language was amended to the protocol.
  - NIH GMS did not request Institutional Certification for Human Genomic Data

- **What is the correct IRB approval date?**
  - System only allows one IRB approval date
  - Protocol amendment and funding sheet, adding R01 as funding source, was submitted to OHRS for congruency review. OHRS issued congruency IRB approval on **1/5/2018**.

Who to Contact?

DFCI IRB (and Privacy Board)	**Emily Eldh, CIP** **Elizabeth Bowie, JD**	Emily_Eldh@dfci.harvard.edu Elizabeth_Bowie@dfci.harvard.edu	Main #: (617) 632-3029
DFCI Contracts & Agreements	**Mary Melloni, RN, JD, MBA**	Mary_Melloni@dfciharvard.edu	
DFCI MTAs	**Anita Ballesteros, PhD**	Anita_Ballesteros@dfci.Harvard.edu	
DFCI Grants & Contracts	**Tina DaSilva, CRA** **Grants Management** **Officer**	Tina_Dasilva@dfci.harvard.edu G&C Staff Listing	
DFCI Research Compliance	**Rachel Rice-Ackman, JD**	Rachel_RiceAckman@dfci.harvard.edu	

QUESTIONS