IRB 101: An Introduction to the WCM IRB

Presented by

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Office of Human Research Compliance
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https://research.weill.cornell.edu/irb
Today's Topics

Office of Human Research Compliance Organizational Chart

Is IRB Review Required?

Preparing and Submitting to the IRB

Things to Know About WRG-HS

What Kind of Review?

Common Causes of Delays

Post Approval Process
Office of Research Integrity

Animal Research

Human Research Compliance

Regulatory Compliance
- Human Embryonic Stem Cell Research
- Immediate Reports
- ClinicalTrials.gov
- Data & Safety Monitoring Committee
- Single IRB & Reliance

IRB
- Cancer IRB
- General IRBs 1 & 2

General Research Compliance

HRP Operations
- Quality Assurance
- Education & Communication
- Research Navigation

Weill Cornell Medicine
IRB review is required for research involving human subjects
What is Research?

**45 CFR 46.102(e):**

- **Research** means a systematic investigation including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

**FDA definition 312.3(b) and 812.3(h):**

- **Clinical investigation** means any experiment that involves a test article and one or more human subjects, and that either requires prior submission to the FDA or when the results will be used to support an application for a research or marketing permit.
- **Test article** means any drug (including a biological product), medical device, food additive, color additive, electronic product, or any other article subject to FDA oversight.
What is a Human Subject?

A living individual about whom an investigator obtains:

- Data through intervention or interaction with the individual, OR
- Identifiable private information

Per the FDA, subject means a human who participates in an investigation:

- Either as a recipient of the new test article or as a control.
  - A subject may be a healthy human or a patient with a disease. [21 CFR 312.3(b)]
- Either as an individual on whom or on whose specimen a test article is used or as a control.
  - A subject may be in normal health or may have a medical condition or disease. [21 CFR 812.3(p)]
### What Regulations Apply?

<table>
<thead>
<tr>
<th>Organization</th>
<th>Regulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>OHRP</td>
<td><strong>Common Rule</strong> <em>(45 CFR §46)</em></td>
</tr>
<tr>
<td>FDA</td>
<td>Device, Drug and IRB regulations <em>(21 CFR §812; §312, §50, and §56)</em></td>
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<tr>
<td>DoD</td>
<td>Instruction 3216.02</td>
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<tr>
<td>Office of Civil Rights</td>
<td><strong>HIPAA</strong> <em>(45 CFR §160 and §164)</em></td>
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<tr>
<td>ICH</td>
<td>International Conference on Harmonisation <em>(ICH) Good Clinical Practice</em></td>
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<tr>
<td>EUGDPR</td>
<td>European Union General Data Protection Regulation</td>
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<tr>
<td>NIH</td>
<td>Imposes requirements on funded research</td>
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<tr>
<td><strong>State, Local, and Institutional</strong> Regulations</td>
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### Approval Criteria (45 CFR 46.111 / 21 CFR 56.111)

In order to approve research involving human subjects, the IRB must determine the following requirements are satisfied:

- Risks to subjects are minimized by:
  1) Using procedures consistent with sound research design, using procedures already done on the subjects for other purposes, and;
  2) Without exposing subjects to unnecessary risk.

- Risk to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be reasonably expected as a result

- Selection of subjects is equitable

- Additional safeguards have been included in the study to protect the rights and welfare of subjects who are vulnerable to coercion or undue influence

- Informed consent will be appropriately documented or appropriately waived in accordance with §46.117(c)

- The research plan has adequate provision for monitoring the data collected to ensure subject safety

- There are adequate provisions to protect the privacy of subjects

- There are adequate provisions to maintain the confidentiality of data

- The informed consent process is adequate

- The documentation of informed consent is adequate
Elements of a Successful Submission

- Well planned protocol
- Completed COI disclosure
- Completed CITI training
- Ancillary Committee(s) approval
- Appropriate informed consent process
- Complete and accurate IRB application
- Approval
- Post-approval compliance
Planning a Protocol

- Every new submission requires a protocol
  - ’protocol’ ≠ ‘application’
- JCTO provides protocol templates for:
  - Observational Correlative Studies
  - Therapeutic Studies
  - Tissue Use/Chart Reviews
- Be aware of IRB policies
  https://research.weill.cornell.edu/compliance/human-subjects-research/institutional-review-board/irb-policies-and-procedures
Conflict of Interest

• All researchers/investigators engaged in human subjects' research must have a current financial COI disclosure on file at the time of protocol submission
• COIs are submitted to the WCM COI Office through the Conflicts Survey in WRG
• COI Disclosures must be renewed annually

To complete a Conflicts Survey:
1. Log into WRG (https://wrg.weill.cornell.edu) with your CWID/password
2. Once in WRG, click on Conflicts of Interest
3. Click on Create/Update Disclosure

Instructions also available here
Educational Requirements

- Biomedical Research Investigators and Key Personnel
  - Refresher course needed after 3 years
- CITI Course in Good Clinical Practice (GCP)
  - Refresher course needed after 3 years

Preparing and Submitting to the IRB

- Well planned protocol
- Completed COI disclosure
- Completed CITI training
- Ancillary Committee(s) approval
- Appropriate informed consent process
- Complete and accurate IRB application
- Approval
- Post-approval compliance
Ancillary Approvals

- **Protocol Review & Monitoring Committee (PRMC)**
  - Cancer PRMC: for cancer-related studies  
    cancerPRMC@med.cornell.edu
  - General PRMC: for all other studies  
    generalPRMC@med.cornell.edu
- **PRMC-equivalent committees**

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Preparation and Submitting to the IRB:

- Well planned protocol
- Completed COI disclosure
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- Ancillary Committee(s) approval
- Appropriate informed consent process
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Informed Consent

- **Think of this as a process**
- **Remember the purpose of the process**
  - To inform: use language that is easy to understand
  - Signed documentation
- **Other options, as appropriate, include:**
  - Waiver of Signed Documentation (e.g., oral consent)
  - Waiver of Informed Consent (e.g., for chart reviews)

Successful Informed Consent = Information + Comprehension + Voluntariness
Oral Consent and Waivers

- **A waiver of signed documentation or a full waiver of consent** is permitted under the regulations in certain circumstances for minimal risk research.
- The research record should still contain documentation of the consent process, including the date and time.
- Consent waivers and HIPAA waivers are two different things!
  - You might satisfy the requirements of one but not the other.
- IRB approval of the oral consent or waiver is required.

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**Preparing and Submitting to the IRB**

- Well planned protocol
- Completed COI disclosure
- Completed CITI training
- Ancillary Committee(s) approval
- **Appropriate informed consent process**
- Complete and accurate IRB application
- Approval
- Post-approval compliance
Accurate IRB Application

• The application must reflect the research and be consistent with information presented in the other submission components (e.g., protocol, consent documents, etc.)

• IRB Review Application (IRA)
  o Biomedical IRA: If using the JCTO Therapeutic Protocol template and/or your study uses a device/drug or implements a clinical trial
  o Biorepository IRA: If establishing a biorepository ONLY
  o Medical Education IRA: If your study is minimal risk and qualifies under exempt category 1
  o SBER and Records IRA: If using the JCTO Observational or Tissue Use/Chart Review template, and/or study is SBER
WRG-HS Electronic Submission System

- All protocols for review by the IRB must be submitted through the Weill Research Gateway Human Subjects portal (WRG-HS):
  - Submission portal for protocols, continuing reviews, amendments, etc.
  - Check status of protocols
  - Edit, amend, and renewal of protocols
  - Reportable events (deviations, lapse requests)
- WRG Comprehensive Job Aid
First things first: Access to WRG-HS (and CT, if applicable)

Modules to have access to:
- Human Subjects (HS)
- Clinical Trials (CT)

Select add for both regulatory coordinator and clinical research associate
WRG-HS Submission

Plan/Draft Protocol
Plan/Draft Consent(s)
Confirm CITI/COI Certification

Complete & Submit IRB Application

Received by IRB for pre-review

Formal IRB Review

Approval!

Returned for stipulations (revisions)

IRB review cannot begin until these steps are complete!
**Categories of Review and Submission Timing**

*Meeting dates are on our webpage*

<table>
<thead>
<tr>
<th>Degree of Risk</th>
<th>Category of Review</th>
<th>WCM IRB Form</th>
<th>Submission Deadline</th>
<th>Typical Turnaround*</th>
</tr>
</thead>
<tbody>
<tr>
<td>minimal</td>
<td>Exempt</td>
<td>WRG-HS</td>
<td>Rolling</td>
<td>~2 weeks</td>
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</tr>
<tr>
<td>&gt; minimal</td>
<td>Full</td>
<td>WRG-HS</td>
<td>Rolling</td>
<td>~2 weeks</td>
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</table>

*Turnaround means first response by IRB. This may be approval, or more often, a request for changes or additional information in order to start a formal review.
Exempt Research

Review Procedure:

• Exempt research requires submission to and verification by the WCM IRB

• Researcher must submit to the WCM IRB:
  o WRG-HS Application and detailed protocol, including required documents

• Exempt studies require an informational sheet (if applicable) to provide relevant information about the study to potential participants

• WCM IRB will issue a formal determination of exemption
Expedited Review

• Research involves no more than minimal risk and procedures listed in one or more of the federally defined categories

• Protocol is reviewed by one or more IRB member
• If protocol is determined to be more than minimal risk, review will send it to full committee review
• A single reviewer may not disapprove the research
  o BUT they may determine that is should have full committee review.
The following human subjects research requires review by a convened IRB:

• Research that does not qualify for expedited review or exemption from federal regulations
• Research that is referred to full board during expedited review by an IRB member
  o For disapproval
• Research involving certain vulnerable populations
How Does Full Board Review Work?

1. Submissions are assigned to a board on a rolling basis once they are determined to be complete.
2. Protocol assigned to two IRB members for detailed review:
   • Reviewers may consult with the PI to resolve issues before the meeting.
3. Reviewers present the protocol to the IRB for discussion:
   • IRB members with COI must recuse themselves.
4. Further discussion followed by a vote to approve, request modifications, or disapprove the protocol.
5. PI is notified of outcome and any required changes for approval.
Full Board Determinations

• **Approved**: Meets regulatory requirements for approval; no changes necessary

• **Modifications required**:
  - Directive changes necessary
  - Substantive changes necessary

• **Disapproved**: The board cannot reasonably imagine revising the study in such a way that the benefits outweigh the risks
Notification of Approval!

Note:
- Approval period*
- Any provisos
- “Stamped” (digitally) documents available in WRG-HS:
  - Consent forms
  - Recruitment material
  - Any other patient-facing materials

*No expiration date in the stamp for PAM-AR eligible studies
Protocol & Informed Consent

- First page of ICF is “stamped”, showing:
  - Approval date (from)
  - Expiration date (to) *
- Re-approval after any changes are made (via amendment)
- Do not let your approval lapse!
  - Submit your renewal at least 60 days before your expiration date
- Most recently approved document must be used at all times
  - Available in WRG-HS
Where Is My Study?
WRG-HS Submission

Plan/Draft Protocol

Plan/Draft Consent(s)

Confirm CITI/COI Certification

Complete & Submit Intake Form, then IRB Application

Pending

Received by IRB for pre-review

Formal IRB Review

Approval!

Returned for stipulations (revisions)

Note: This includes several pre-IRB steps including: PI, chair, and other sign-offs, and ancillary reviews. Track submission progress!

Confirm CITI/COI Certification

IRB review cannot begin until these steps are complete!

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Common Causes For Delays

- Submission not fully submitted
  - e.g., still in draft, signature routing not completed correctly, etc.
- Missing PRMC approval
- CITI not current for key personnel
- COI not current for key personnel, if applicable

- Incomplete/inaccurate/inconsistent submission
- Slow responses to stipulations
- Common WRG errors:
  - Application errors (read the questions carefully)

Missing/incorrect/incomplete answers in your WRG application, and/or the absence of required documents, will delay your review!
Tip #1: Complete the WRG-HS Training

- Book a training
- Consult the WRG-HS Knowledge Base documents
- Make sure your CITI account is linked to your WRG-HS email that your training is up to date
- Make sure your COI survey is submitted

It looks like you’re submitting an IRB application. Need some help?
Tip #2: Avoid Incomplete or Sloppy Paperwork

- Remove all help text and irrelevant sections from consent form templates
- Include ALL documents:
  - Data collection tool
  - Recruitment flyers
  - FDA documentation
  - etc.
Tip #3: Avoid Discrepancies!

The IRB pays close attention to detail and cannot process submissions when discrepancies exist!

Example 1
IRB application states the PI is requesting a QI determination but the protocol describes the project as a research study

- The IRB follows a very specific federal definition of what qualifies as research. It’s important for the IRB to understand the intent of the PI but also to ensure consistency across documents (since the research vs. QI determination impacts regulatory requirements for the PI and the institution.)

Example 2
Protocol states no identifiers will be collected; data collection tool indicates that dates of service will be collected

- Dates are indirect identifiers under HIPAA
- The IRB is also a HIPAA privacy board so will ask you for a detailed data collection tool in order to make HIPAA determinations
**Tip #4: Describe Recruitment in Detail**

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<tr>
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</thead>
<tbody>
<tr>
<td>• Any secondary subjects involved?</td>
<td>• Appropriate institutional permission in place?</td>
<td>• Rationale for including or excluding certain populations?</td>
<td>• Consider potential for undue influence or coercion</td>
<td>• Which individuals will conduct consent?</td>
</tr>
<tr>
<td>• Proxy or LAR consent?</td>
<td>• Does location of recruitment cause risk to subject or chance for undue influence or coercion?</td>
<td></td>
<td></td>
<td>• How will you notify potential participants about a study?</td>
</tr>
<tr>
<td>• Parental permission?</td>
<td>• Any international or state laws to consider?</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

It looks like you’re submitting an IRB application. Need some help?
Tip #5: Describe the Flow of Information

- If the institution receives or shares identifiable information for human subjects research purposes, IRB review is required.
- If the institution sends out PHI for human subjects research purposes, the IRB must verify that a valid HIPAA Authorization is in place to allow the disclosure:
  - Or, the IRB may approve a waiver of HIPAA Authorization.
  - For non-HRS purposes, contact the Privacy Office.
- DUAs and/or MTAs may be required prior to sending or receiving data and/or specimens.
- Please describe very clearly what, exactly, is being sent where.
Protected Health Information Identifiers

Reminder: Dates and zip codes or other geographic indicators are indirect HIPAA identifiers. Data that contains dates, zip codes, etc., is not considered de-identified under HIPAA
Tip #6: List all External Sites

• List all sites involved in the research including coordinating centers and protocol sites

• External collaborators working on human subjects research need IRB approval
  o IRB approval should be obtained through the collaborator’s home institution or through the WCM IRB
  o For federally-funded, non-exempt research, a reliance agreement must be in place. Please email reliance@med.cornell.edu to set up reliance agreements or for questions related to single IRBs/collaborators
Tip #7: Clearly Distinguish between Research and Standard of Care

• Generally speaking, the protocol and consent should describe the risks and benefits associated only with the research and not any related SOC procedures.

• The IRB weighs the risks and benefits of research procedures only, and approval will be delayed if it is not clear to the IRB which procedures are part of standard of care and which are for research purposes only.

• Please describe research procedures and SOC clearly and chronologically.

It looks like you’re submitting an IRB application. Need some help?
Tip #8: Include a Data Analysis Plan

• Is the sample size adequate to answer the research question and to justify putting subjects at risk?
• Is the data analysis appropriate for the question being asked?
Tip #9: Make Sure Your FDA Paperwork is Up To Date

- If you are the sponsor investigator, as defined by the FDA, please be sure your IDE or IND paperwork is up to date (including amendments for any new protocols submitted to the IRB)
- For assistance with FDA paperwork or questions about FDA regulated research, please submit an IRB Training and Consultation Request here
Tip #10: Ensure your ICF Meets IRB Expectations

1. WHAT IS IT ABOUT?
A statement about, and description of, the study

2. WHAT ARE THE RISKS?
A description of risks or discomforts to the subject

3. WHAT ARE THE BENEFITS?
A description of any benefits to the subjects

4. ARE THERE ALTERNATIVES?
A disclosure of appropriate alternative procedures or courses of treatment

5. WHO WILL KNOW?
A statement describing how confidentiality will be maintained

6. IS THERE COMPENSATION?
For greater-than-minimal risk studies, compensation and/or medical treatment

7. WHO IS THE CONTACT?
Contact information for questions or more information

8. IS IT MANDATORY?
A statement that participation is voluntary

9. WHAT HAPPENS AFTER?
A statement about what will be done with collected information

It looks like you’re submitting an IRB application. Need some help?
For more on the ICF…

It looks like you’re writing an ICF. Need some help?
For more Tips and Tricks…

It looks like you’re submitting an IRB application. Need some help?
Ongoing (Post-Approval) Requirements

- Advertisements and amendments must be reviewed *prior to* implementation
- Continuing review required for re-approval
- Protocol exception requests for planned, one-time deviation from protocol
- Reportable events must be reported within 5 business days
- Everything is submitted in WRG

Post Approval Process

- Well planned protocol
- Completed COI disclosure
- Completed CITI training
- Ancillary Committee(s) approval
- Appropriate informed consent process
- Complete and accurate IRB application
- Approval
- Post-approval compliance
Protocol Recertification: Continuing Review & PAM-AR

• On-going research must be re-reviewed at intervals appropriate to the degree of risk, at least once per year
• PI is notified in advance of the due date
  o Notifications emailed 90, 60, & 30 days before, and on, the expiration date
• All research must halt once IRB approval expires
  o Remember: maintenance of identifiable data is considered research activity!

*If you have a reliance agreement in place and we are NOT the IRB of record, research does not have to be halted as long as a CR/PAM-AR has been submitted to the WCM IRB within 2 weeks of the IRB of record’s CR/PAM-AR approval
Events must be reported to the IRB within 7 calendar days:

- Unanticipated Problems
- Protocol deviations
- Breach of confidentiality (*within 24 hours*)
- Action taken to eliminate an apparent immediate hazard to subjects
- Other events listed in the policy, found [here](#)
What
We’ve
Covered

Office of Human Research Compliance
Organizational Chart

Is IRB Review Required?

Preparing and Submitting to the IRB

Things to Know About WRG-HS

What Kind of Review?

Common Causes of Delays

Post Approval Process
How can the IRB staff help you?

- Update IRB website to include up-to-date policies, procedures, and guidance documents
- Be available for consultation services when needed, especially for new research staff
- Review the submission early enough to send requests for modifications or clarifications during the pre-review
- Send the submission to the fully convened IRB with pre-review questions answered so that the outcome review and discussion (full committee) requires only minimal modifications
- Send timely and complete approval letters
Resources

Office of Human Research Compliance website

https://research.weill.edu/irb

Includes: Policies and Procedures
Submission Guidelines
Educational Materials
Staff Directory

Visit our Human Research Compliance Monthly Education and Training Series (METS) page to watch recordings of our past METS presentations!

Need help? We are here for you!

WCM IRB Office: irb@med.cornell.edu
HRPO team: hrpo@med.cornell.edu
WCM IRB Contact Information

irb@med.cornell.edu

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