

## Welcome to our September METS

- Please make sure your microphones are muted
  - There will be a Q&A session after this presentation
    - Please reserve your questions until then
- OR
- Put any/all questions in the chat and we will address them after the presentation
  - This session may be recorded



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**Weill Cornell  
Medicine**

# IRB 101: Regulating Research

Research Ethics and the Responsible Conduct of Research



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<https://research.weill.cornell.edu>



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# Human Subjects Research Ethics

**Researcher responsibility to be honest and respectful to all individuals who are affected by their research studies or their reports of the studies' results**

**At every step of the process:**

- Responsibility to ensure the **welfare** and **dignity** of human and non-human participants/subjects in the study
- Responsibility to the discipline of science to be **accurate** and **honest** in public reports



## Why Ethics?



## The Nuremberg Trials (1946-47)

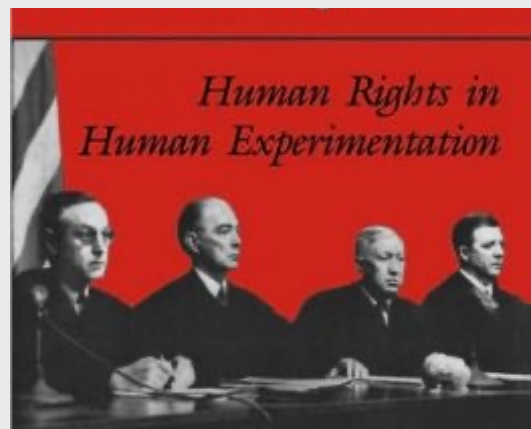
- **The Doctors' Trial exposed Nazi experimentation on human subjects**
  - Infection of soft tissues
  - Freezing/hypothermia studies
- **Laid the groundwork for today's psychological and medical ethical standards**



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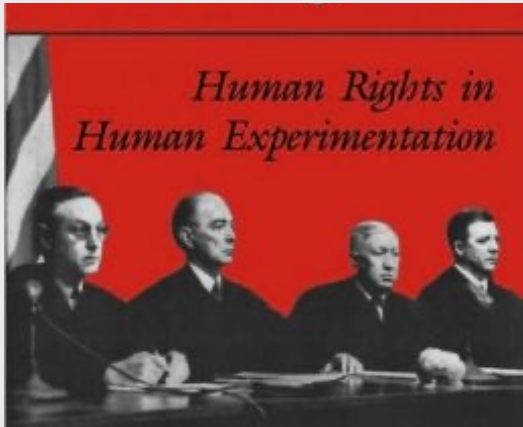
## 10 Points of The Nuremberg Code

1. **Voluntary consent of human subject is essential**
2. **The experiment must be necessary and yield fruitful results for the good of society**
3. **The experiment must be designed and founded on prior knowledge so that the anticipated results will justify the performance of the experiment**
4. **Avoid all unnecessary physical and mental suffering/injury**
5. **No experiment should be conducted when you know death or a disabling injury will occur (unless the experimenters also participate!)**



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## 10 Points of The Nuremberg Code, Cont.



6. The risk should never outweigh the benefit
7. Protect the participants from even remote possibilities of injury, disability, or death
8. The experimenter must be qualified to conduct the experiment
9. The subject has the right to terminate his/her involvement at any point during the experiment
10. The experimenter must be willing to terminate the experiment when/if he suspects injury, disability, or death might occur



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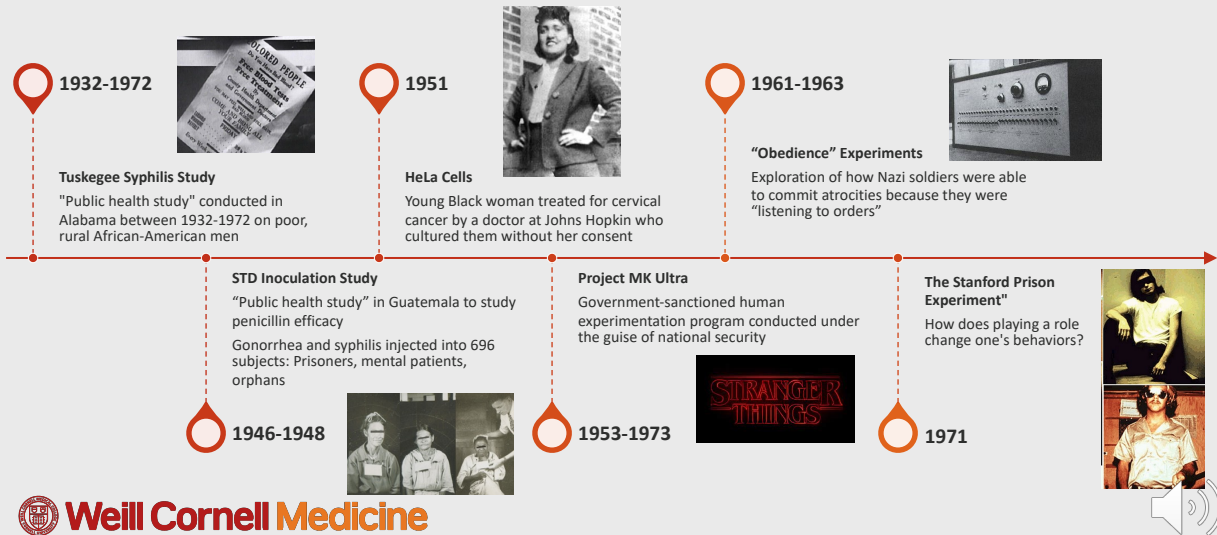
No more unethical studies, right?

Wrong.



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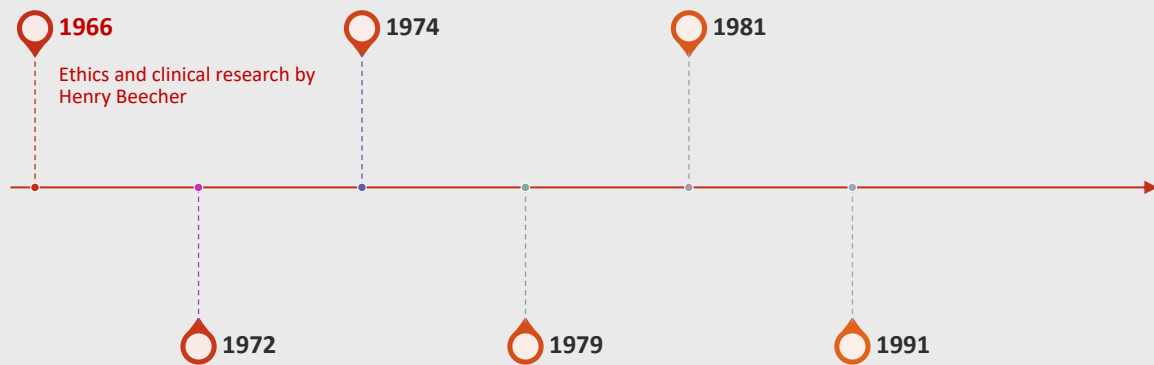
## A Brief History of Human Subjects Violations



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## A Brief History of Human Subjects Protection

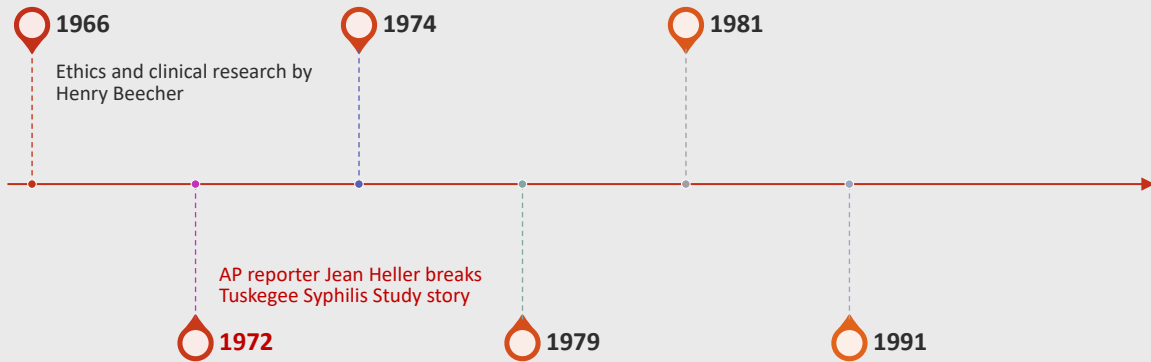


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## A Brief History of Human Subjects Protection



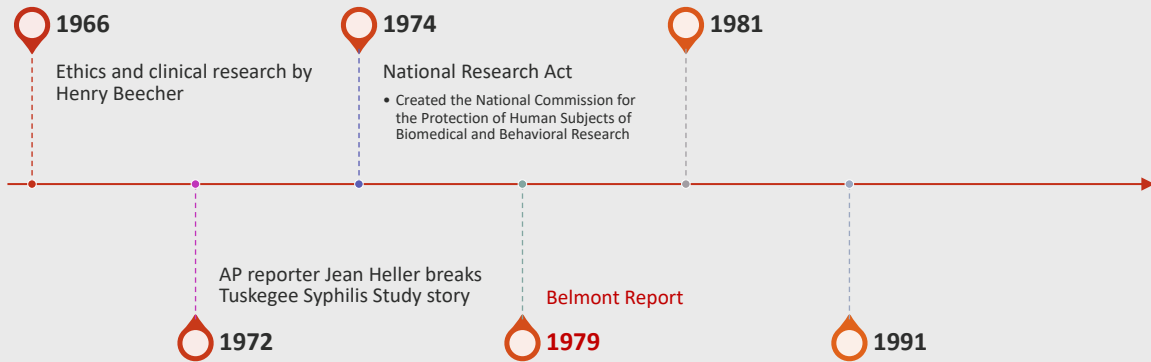
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## A Brief History of Human Subjects Protection



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## A Brief History of Human Subjects Protection



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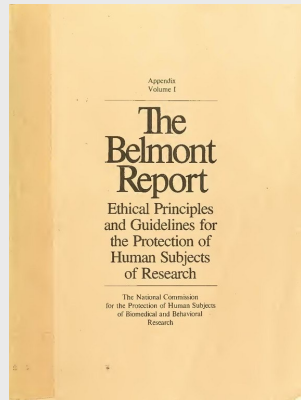
# Advisory Panel Convened in 1972

The Belmont Report



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# Basic Ethical Principles



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## Respect for Persons

- Individuals should be treated as autonomous agents
- Persons with diminished autonomy are entitled to special protection
- Application:

- Requirements of voluntary, informed consent
- Maintain confidentiality and privacy
- Extra protections for vulnerable populations

### §46.111 Criteria for IRB approval of research.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by, [§46.116](#).

(5) Informed consent will be appropriately documented or appropriately waived in accordance with [§46.117](#).

(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(b) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

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# Beneficence

- **Two general complementary rules:**

- Do no harm
  - ❖ All research has the prospect of harm, even if minimal
- Maximize possible benefits and minimize possible harms

## §46.111 Criteria for IRB approval of research.

(a) In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:

(1) Risks to subjects are minimized:

- (i) By using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk, and
- (ii) Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

(2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

# Justice

- **Fairness in the distribution of the benefits and burdens of research**
  - Seeks to guard against the unfair selection of research subjects because of their availability, compromised position, or manipulability
- **The principle of justice requires that equals are treated equally, and non-equals are treated non-equally (e.g., how we treat an infant vs. an adult)**

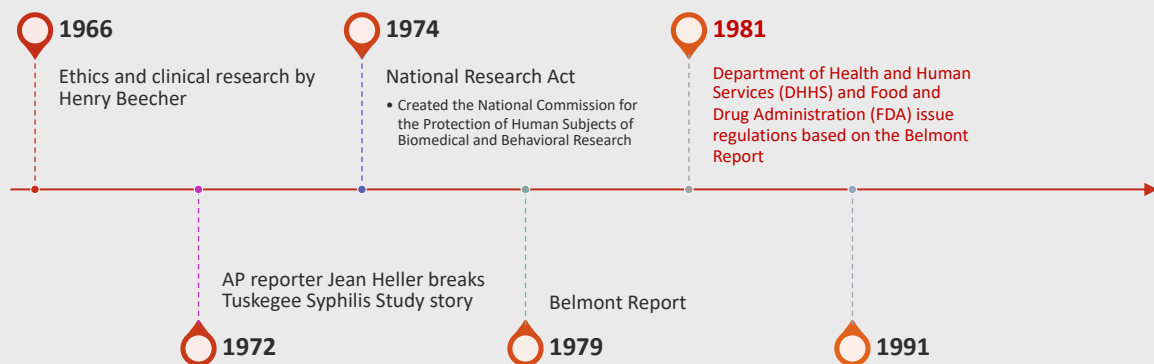
## §46.111 Criteria for IRB approval of research.

(3) Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted. The IRB should be particularly cognizant of the special problems of research that involves a category of subjects who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.

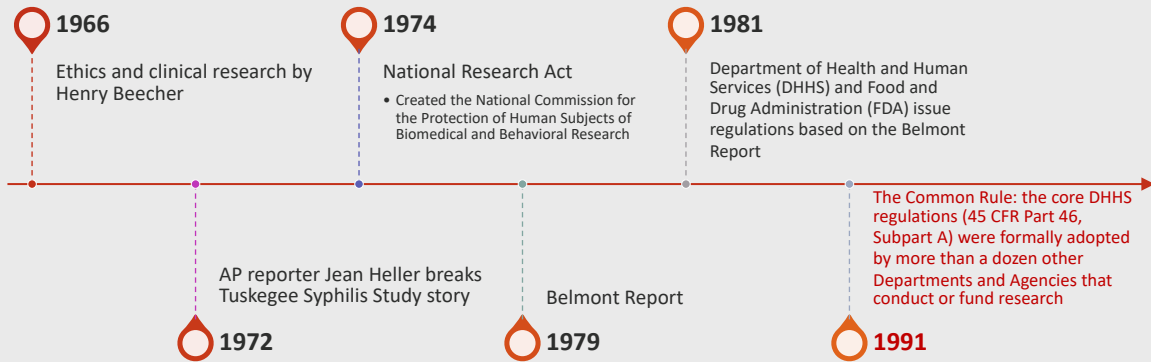
## Note:

- The Belmont Report was issued by a committee based solely in the United States
  - Individualism is #1!
- Consider ethical principles of other cultures
  - Value of complex relationships
  - Benefit to society/family overriding autonomy
  - Paternalism

## A Brief History of Human Subjects Protection



## A Brief History of Human Subjects Protection



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## Research Ethics vs Research Regulation

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## Regulation vs. Guidance



### Regulation (Law)

Federal/state requirements  
*must* be complied with



### Guidance (Ethics)

Best practices recommended by  
the agency; optional

### Policy

Institutional requirements *must* be complied with

## Research vs. Clinical Care

	Clinical Care	Research
Purpose	provide personal care for particular patients	generalizable knowledge
Methods	none	randomization, blinding, placebo controls, protocols restricting treatment flexibility, washout periods, and research procedures to measure study outcomes
Justification of Risks	potential medical benefits to patients	anticipated value of knowledge
Relationship	Fiduciary relationship with patient	Primary obligation to research

## What Regulations?

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

## Office of Human Research Protections (OHRP)

### Depends on your FWA (Federalwide Assurance)

- Written documentation of an institution's commitment to comply with federal regulations governing (federally supported) human subjects research
- Each legally separate entity must have its own FWA
  - Includes:
    - Statement of ethical principles
    - An assurance of compliance for all federally supported research
  - **Technically only required for federally supported research**
    - NY State Regulations – essentially require extension to all research

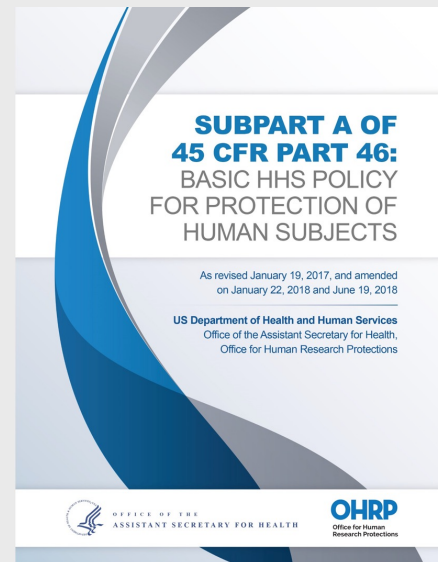
## Common Rule (45 CFR §46, Subpart A)

### Requirements for:

- **Assuring compliance by research institutions**
- **Researchers obtaining and documenting informed consent**
- **Institutional Review Board (IRB) membership, function, operations, review of research, and record keeping**

### Additional protections for certain vulnerable research subjects (outside the Common Rule):

- Pregnant women, fetuses, and neonates (Subpart B)
- Prisoners (Subpart C)
- Children (Subpart D)



## At WCM/NYP



**Apply the Common Rule to all research**

**Apply the additional protections for pregnant women, fetuses, neonates, and children to all research**

**Send prisoner research to an external IRB (BRANY) to review**

## Federal Drug Administration (FDA)

- **Title 21, Parts 50, 56, 312, 812**
- **Regulations for research involving FDA regulated drugs, devices, biologics**
  - New
  - Changing marketing or labeling
- **Data Safety Monitoring Board**
  - Required for all clinical trials
  - 5-10 experts review data every 6 to 12 months
  - Independent board

## When Do FDA Regulations Apply?

- **Clinical Investigation instead of research**
- **Test article, what's that?**
- **Not your typical human subject...**



## FDA Exceptions for Obtaining Informed Consent

Life-threatening conditions that meet all of the following:

- Investigator and another physician believes the situation necessitates the use of a test article
- Subject or representative cannot consent
- Insufficient time to obtain consent
- No alternative available that provides an equal or better chance of survival

## Differences between OHRP & FDA Regs

- FDA has not adopted the Common Rule
- Consult with your IRB analyst if you are unsure which ones apply



For a comparison of regulations, go to:  
<https://www.fda.gov/science-research/good-clinical-practice-educational-materials/comparison-fda-and-hhs-human-subject-protection-regulations>

## Health Information Portability and Accountability Act (HIPAA)

- **Authorization to view protected health information (PHI) in medical records**
- **Authorization for disclosure of PHI ≠ Consent for research**
- **Waiver of authorization possible**
- **Are you a covered entity?**
  - A health care provider who transmits any protected health information in connection with a transaction covered by HIPAA (claims, benefit eligibility inquiries, referral authorization requests, et al.)
  - HIPAA guidance: <http://privacyruleandresearch.nih.gov/>
- **Consider research conducted at *either* WCM or NYP to be under a covered entity**

## International Conference on Harmonisation (ICH)

**International Conference on Harmonisation (ICH) Good Clinical Practice (GCP)** is an international standard for the design, conduct, monitoring, and reporting of clinical research.

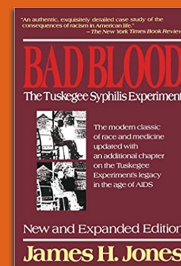
- **FDA considers ICH-GCP to be guidance only**
- **Conducting research in a country regulated by ICH**
- **Conducting research under a contract that binds you to the ICH**

# General Data Protection Regulation (GDPR)

- European privacy law that regulates processing of all “personal data”
- When should you care?
  - Research taking place in the EU or using data from the EU
  - Research sponsored by an EU-based company
  - Are the subjects physically located in the EU (regardless of citizenship)?
- Very particular requirements for consent or “waiver” (more stringent than HIPAA)

## Is it over?

Could Tuskegee Happen Again?  
Could HeLa?



## Why we think it can...

- Are there other areas where treatment options are changing?
- Are there other areas where our understanding of the ethics are changing?
- To what extent is the concept of “ethical research” relative?

## Evidence it has happened...



# So, what keeps us honest?



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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 of 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



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# Institutional Review Board (IRB)

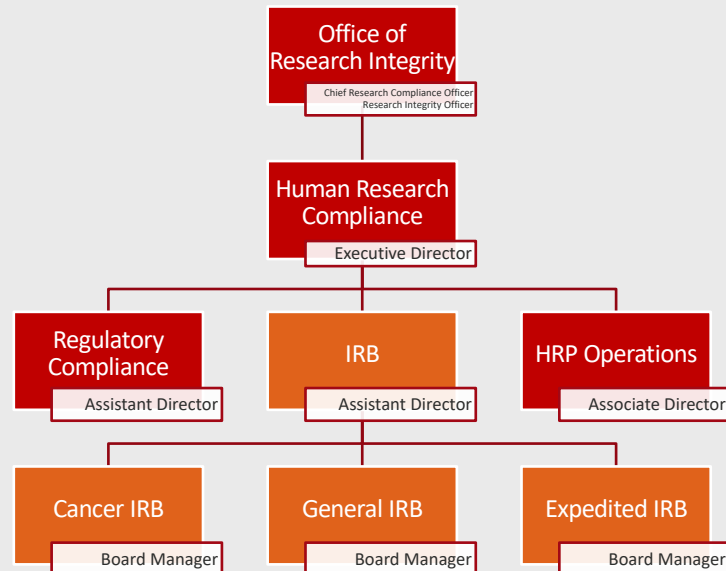
*Headed by scientists/nonscientists in any institution/agency conducting research with human participants*

1. Minimization of risks to participants
2. Reasonable risk in relation to benefits
3. Equitable selection
4. Informed consent
5. Documentation of informed consent
6. Data monitoring
7. Privacy and confidentiality

IRB review is required for **research** involving **human subjects**



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## For More Information on the WCM IRB

Watch our IRB 101: An Introduction to the WCM IRB recording on METS page <https://research.weill.cornell.edu/institutional-review-board/educational-resources/human-research-compliance-monthly-education-and>

### Educational Resources

Explore...

Human Research Compliance Monthly Education and Training Series (HRC METS)



#### Human Research Compliance Monthly Education and Training Series (HRC METS)

The Office of Human Research Compliance is pleased to offer a monthly education and training series for our stakeholders. The goal of this program is to provide a rotating series of sessions that will assist you in making sure your team receives the information they need to navigate the IRB process. If you missed our first session on IRB101: An Introduction to the WCM IRB, you can watch the video here (coming soon).

We hope you can join us for our next session:

**Regulating Research: Ethics and the Responsible Conduct of Research**

Thursday, September 15th, 2022

#### Educational Resources

- HRC METS
- CITI Access Information
- HRC Training and Educational Videos

#### Helpful Links

- Office Directory
- IRB Meeting Resources



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