Ethical Challenge with Human Subjects Research Involving Communities

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Step 1: Answer Key Questions

- **What is human subjects research?**
- **Why do human subjects research?**
- **What makes human subjects research ethical?**

Pop quiz: HSR or no?

Green roofing education

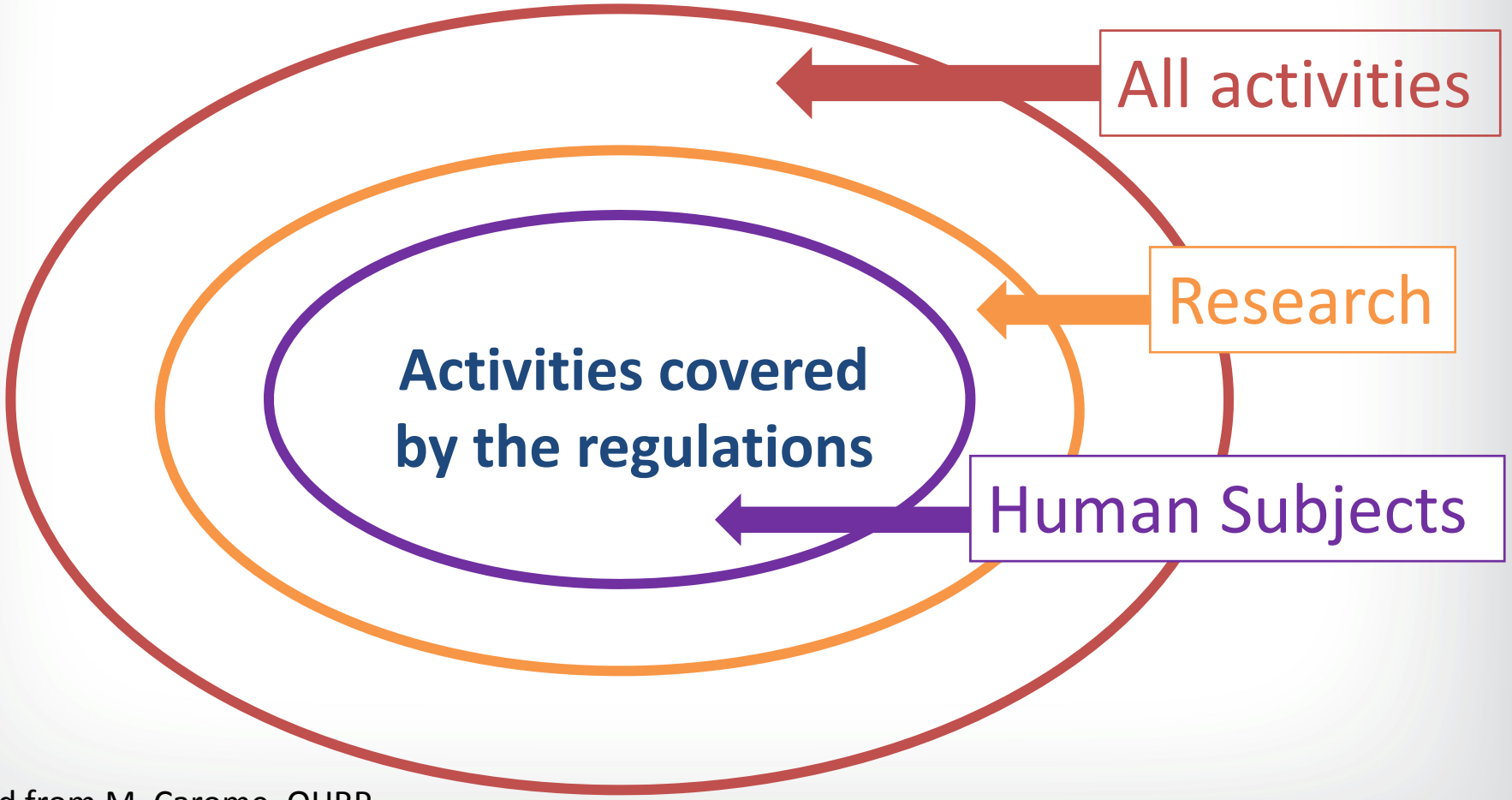
Focus Group

Interview / Citizen Science

Administer a survey

What is human subjects research?

Drawing the Lines with Key Definitions



Adapted from M. Carome, OHRP

Line 1: Definition of Research

A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

[40 CFR 26.102(d)]

Systematic

- Is there a clear study design?
  - Hypothesis?
  - Randomization?
  - Comparison of two products/processes?
- Is there a plan for methodical subject recruitment?
- Are investigators stratifying subject demographics?
- Are the results going to be compared to historical controls/literature?

Designed to develop/contribute to generalizable knowledge

- **Will the activity/project expand scientific understanding or the knowledge base of a scholarly field of study?**
- **Will the project form the basis for or add to the understanding of a particular discipline?**
- **Are you planning to disseminate this information to others to inform policy?**
- **Will you share your findings so that they can be applied to populations outside of the specific study population?**

Note: "intent to publish" may be an insufficient criterion to determine whether or not the project constitutes "research"

Is this research?

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Line 2: Definition of Human Subject

A living individual about whom an investigator conducting research obtains:

(1) Data through intervention or interaction with the individual;

OR

(2) Identifiable private information.

[40 CFR 26.102(f)]

Do the Activities Involve Intervention or Interaction?

Intervention

- Physical procedures by which data are gathered
- Manipulations of subject or subject environment for research

Interaction

- Communication or interpersonal contact between researchers and subject

If "Yes" to either column: it does not matter whether there are identifiers → your research involves human subjects

Is the Information private and individually identifiable?

Private

- Information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place.
- Information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).

Individually Identifiable

- Can the PI or research team "readily ascertain" the subject's identity?
- Can the subject's identity be associated with information?
  - Anonymous Vs. Coded Vs. Identifiers?

Private information must be individually identifiable in order for obtaining the information to constitute research involving human subjects

Are human subjects involved?

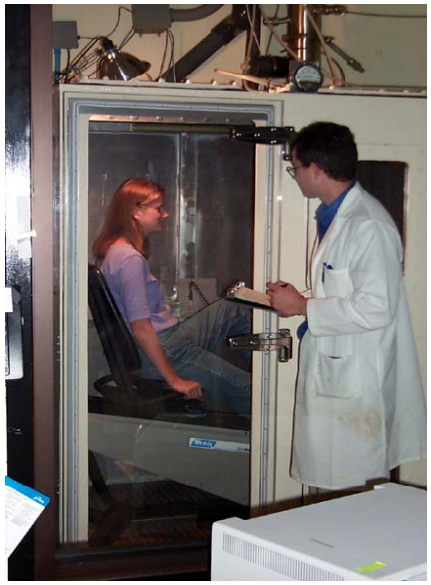
Focus Group

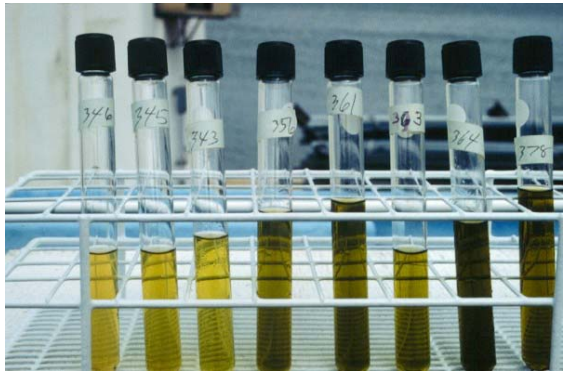
Interview/
Citizen
Science

Administer a survey

Why do human subjects research?

Value of human subjects research





Examples of HSR at the EPA

Intramural Studies

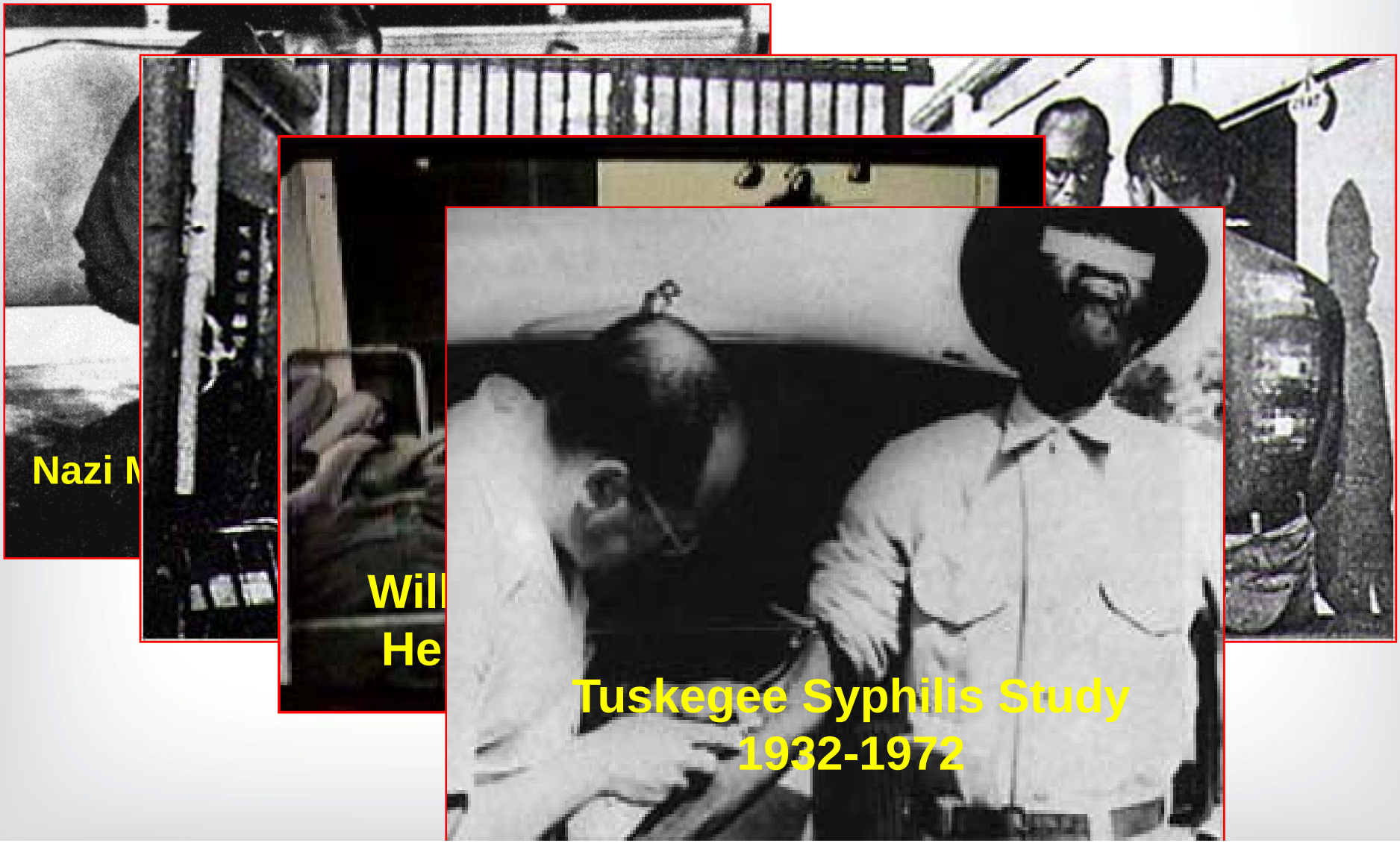
- Controlled exposures
- Epidemiology
- Lead exposure
- Surveys about:
  - Fish consumption
  - Household practices
  - Asthma in kids
  - Education

Extramural Studies

- Sustainable sanitation
- Integrating water and energy engineering and ecotourism
- Reducing traffic congestion

What makes human subjects research ethical?

Concerns for protecting subjects evolved out of a long history in which people were abused in the name of science



US National Research Act, July 1974

- Established *National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research* (1974-1978)
  - The Belmont Report (1979)
- Code of Federal Regulations (1981)
  - Institutional Review Boards (IRBs)
  - Informed consent
- Common Rule (1991)

Public Law 93-348

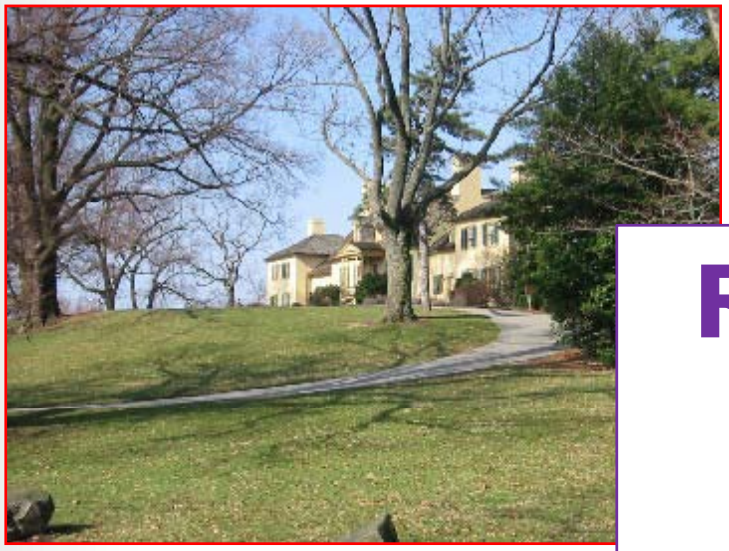
Charge to the National Commission

- *Identify the basic ethical principles which should underlie the conduct of biomedical and behavioral research involving human subjects*
- *Develop guidelines to assure that such research is conducted in accordance with those principles*

National Research Act, 1974 (PL 93-348)

The Belmont Report

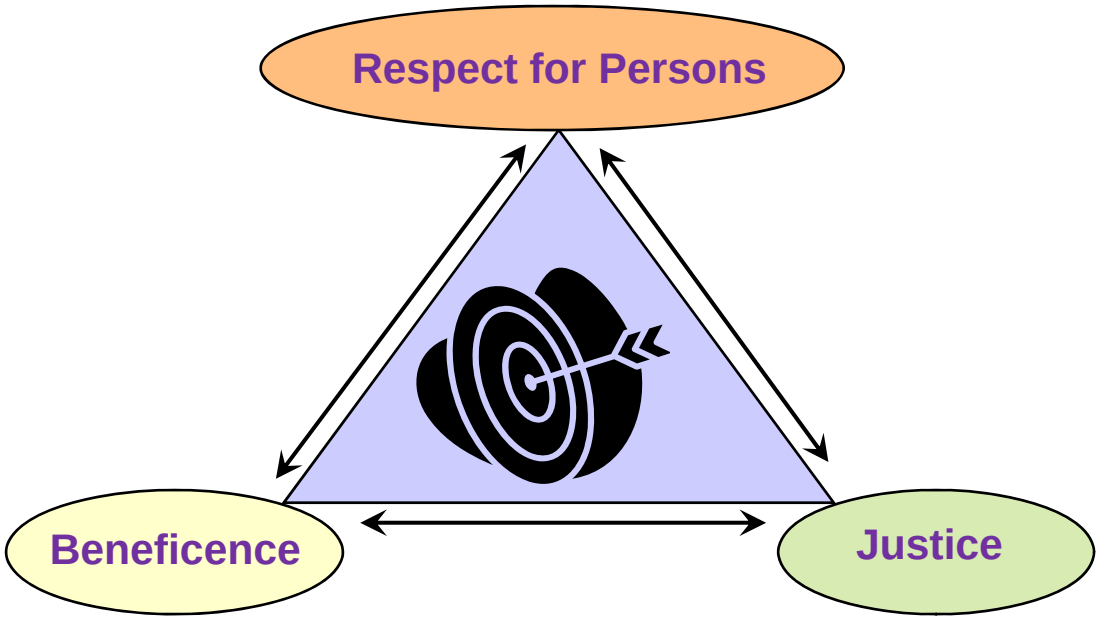
Ethical Principles and Guidelines for the Protection of Human Subjects of Research



Respect for Persons
Beneficence
Justice

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979

Conflict Among Ethical Principles



- Principles carry equal moral weight
- This tension was anticipated and expected
- Requires subjective judgment calls
- Reasonable people will disagree

What makes research ethical?

1. **Collaborative Partnerships**
2. **Value-enhance health or knowledge / Social Value**
3. **Scientific validity**
4. **Fair subject selection**
5. **Favorable risk-benefit ratio**
6. **Independent Review**
7. **Informed Consent**
8. **Respect for enrolled subjects**

E. Emanuel, D. Wendler, C. Grady (2000). What Makes Clinical Research Ethical? JAMA 283.20: 2701-2711.

E. Emanuel, D. Wendler, C. Grady (2008). An Ethical Framework for Biomedical Research in The Oxford Textbook of Clinical Research Ethics. Edited by E. Emanuel et al. New York: Oxford University Press.

(1) Collaborative Partnerships

- **Research is done WITH people, not TO them**
- **Helps guard against exploitation**
- **Helps ensure fair benefits**
- **Helps ensure community determines the priority of research topics and the appropriateness of the research plan**
- **Pragmatic import**

REQUIRES:

- **Partners**
- **Collaboration: shared responsibility**
- **Mutual respect: aspires toward equality**
- **Fair distribution of benefits and awards among community partners**

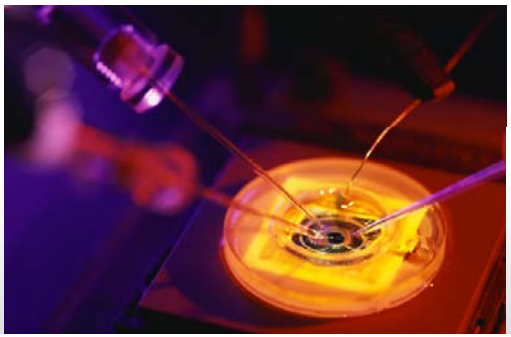
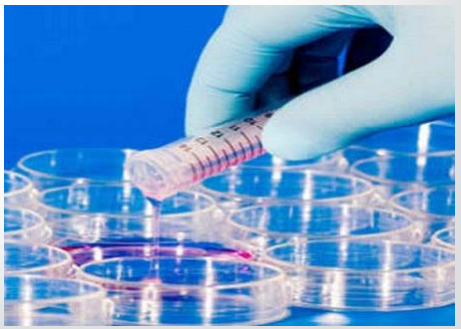
(2) Social Value (Value enhance health or knowledge)

- **Necessary for:**
  - **Improvements in health care or society**
  - **Responsible use of finite resources**
  - **Avoidance of exploitation**

- **Must consider:**
  - **To whom the research will be valuable**
  - **The potential value of research for each beneficiary**
  - **Development of mechanisms to enhance this value**
  - **Impact on current infrastructure**

(3) Scientific Validity

- **General criteria:**
  - **Methods valid and practically feasible for its social, political, and cultural environment**
  - **Clear scientific objective/valid hypothesis**
  - **Design uses accepted principles, methods, practices**
  - **Sufficient power**
  - **Plausible data analysis plan**
  - **Generate useful results**
  - **Cannot deny participants to health care to which they are entitled, nor can providers offer unfeasible services**

(4) Fair subject selection

- **General requirements:**
  - **Scientific goals of study determine inclusion criteria**
  - **No exclusion without scientific reason**
  - **Minimize risks and enhance benefits to subjects**
  - **Fair sharing of risks and benefits**
  - **Enhanced social value of research and benefits to participants**
  - **Consider vulnerability**

(5) Favorable risk-benefit ratio

Favorable risk-benefit ratio

- 3 essential conditions:
  - Potential risks to individual subjects are minimized
  - Potential benefits to individual subjects are enhanced
  - Potential benefits to individual subjects and society are proportionate to outweigh the risks

- Additional considerations:
  - Risks/benefits from research only
    - Extraneous benefits (payment, health services) don't count
  - Type, probability, and magnitude of risks/benefits listed
  - Risks and benefits should be compared

(6) Independent Review

- **Necessary to:**
  - **Guard against conflicts of interest**
  - **Ensure broader considerations**
  - **Promote social accountability**

- **Accomplished through:**
  - **Compliance with applicable laws and regulations**
  - **Independent, competent review: IRBs, DSMCs, etc.**
  - **Transparent review**
  - **Multiple independent reviews when required/justified**

Criteria for IRB Approval

1. **Risks minimized**
2. **Favorable risk: benefit ratio**
3. **Equitable selection of subjects**
4. **Informed consent sought**
5. **Informed consent documented**
6. **Monitoring plan for safety**
7. **Privacy and confidentiality protected**
8. **Additional safeguards for vulnerable populations**

45 CFR 46.111, 21 CFR 56.111, 40 CFR 26.111
(applies to both expedited and convened meeting review)

(7) Informed Consent

- **Necessary for:**
  - **Respect for persons**
    - **Research participation is entirely voluntary**
  - **Beneficence**
    - **Ensuring research participation is consistent with subjects' goals and values**

- **Process includes:**
  - **Information**
  - **Voluntary Choice**
  - **Capacity to Consent**

Process of informed consent

- **Information**
  - **Disclosure of risks and benefits**
  - **Delivery in usable terms**
  - **Continuing access**

- **Capacity to Consent**
  - **Age and Understanding**
  - **Proxy Decision-making**
  - **Vulnerable Populations**
- **Voluntary Choice**
  - **Real deliberation must be possible**
  - **Incentives vs. Undue Inducements (specific to environment)**
  - **Withdraw at any point**

(8) Respect for Participants

- **Considerations beyond informed consent:**
  - **Provision of new information**
  - **Monitor (and act on) subject well-being**
  - **Respecting subject privacy**
  - **Withdrawal without penalty**
  - **Post-trial access to services**
  - **Return of research results**

What are some of the challenges we face in conducting and overseeing studies involving communities?

What's at stake?

Challenges with Communities

- **Study Design**
  - **Minimizing risk: Sensitivity to context**
- **Recruitment**
  - **Process sensitive to community (HIV example)**
- **Informed consent**
  - **Language**
  - **Cultural context (Havasupai example)**
  - **Continual access to information**
- **Evidence of partnership**
  - **Matching expertise of researchers and priorities of communities**
  - **Letters from community organizations**
  - **Tribal approvals**
- **Protection of privacy in the community setting**
- **Community-specific concerns**

What other obligations do we have?

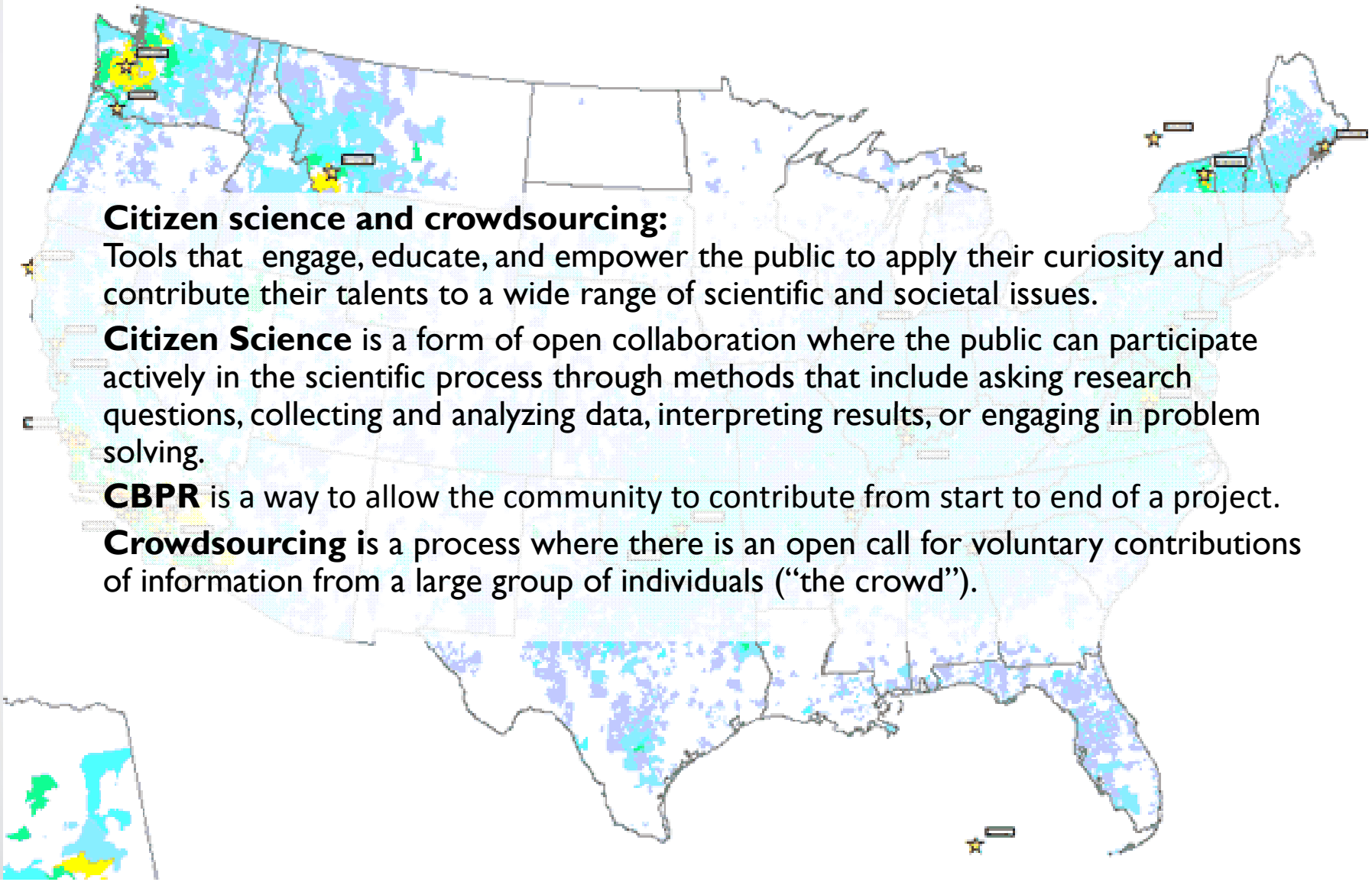
Community Settings

- **Roles and Responsibilities: Whose community? Whose voice? Whose priorities?**
- **Implications of:**
  - **Respect for Persons**
  - **Beneficence**
  - **Justice**
- **Community Collaborations: Ensuring Robust Partnerships**
- **Intent of the research/researchers**
- **Clarifying expectations of:**
  - **Partners**
  - **Participants**
  - **Outcomes**
- **Ongoing collaborations**
- **Representation of communities in results: analysis and publication**

Case Studies

Step 2: Remaining Issues

- What is citizen science and crowdsourcing? What are the ethical issues I should attend to if my research involves these processes?
- What are the regulations we have to follow?
- What is the EPA approval and submission processes like?
- Are there any tips for working with my IRB?



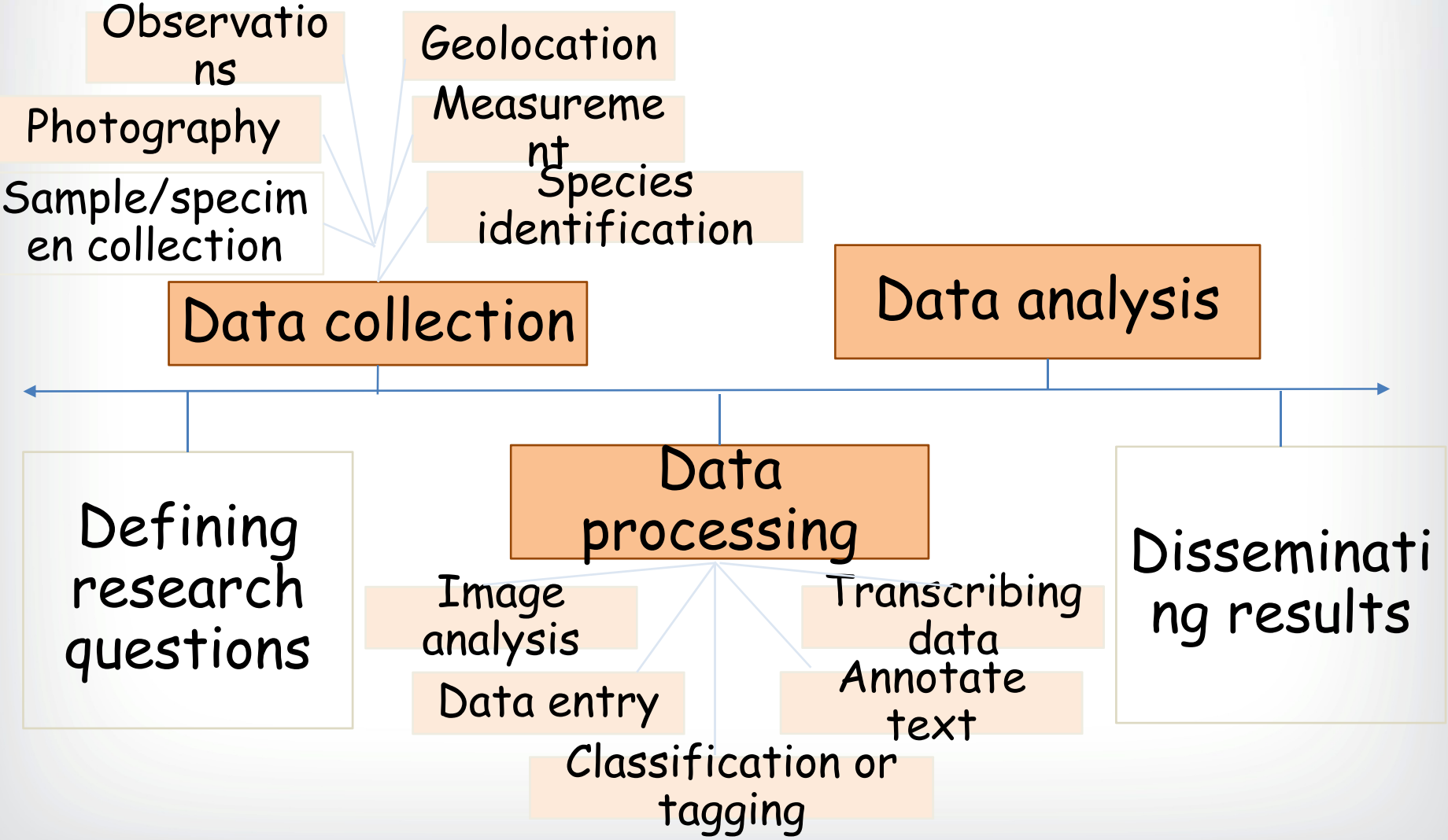
Citizen science and crowdsourcing:
Tools that engage, educate, and empower the public to apply their curiosity and contribute their talents to a wide range of scientific and societal issues.

Citizen Science is a form of open collaboration where the public can participate actively in the scientific process through methods that include asking research questions, collecting and analyzing data, interpreting results, or engaging in problem solving.

CBPR is a way to allow the community to contribute from start to end of a project.

Crowdsourcing is a process where there is an open call for voluntary contributions of information from a large group of individuals ("the crowd").

Participation by citizen scientists



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Ethical Issues: HSR and Citizen Science

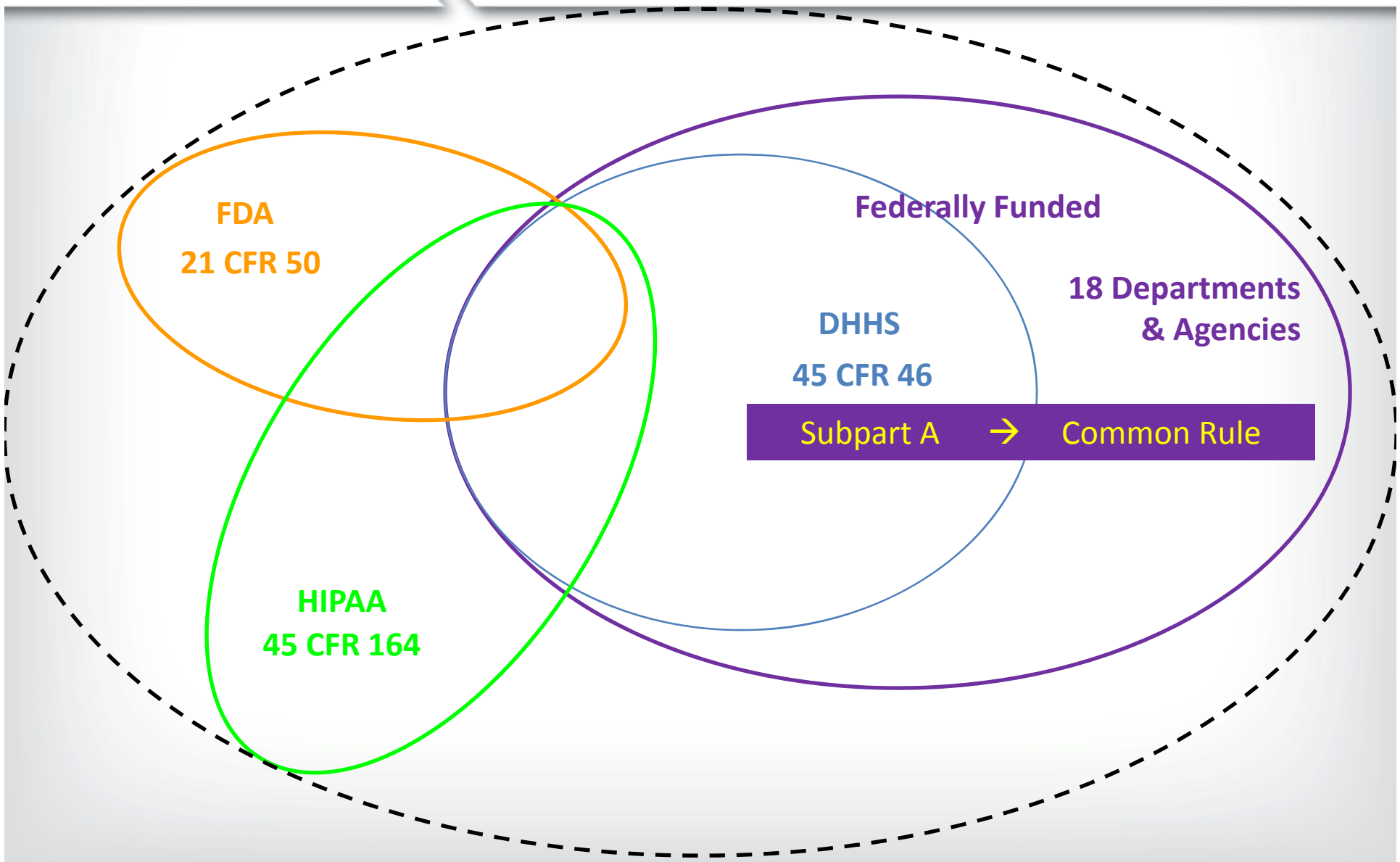
- **Proper Training on issues of HSR**
  - **Good data**
  - **Respecting privacy of other participants**
  - **Collecting PHI/PII**
- **Transparency about the project**
  - **Short term and long term goals**
  - **Return of research results**
- **Cultural/Community Context**
  - **Language**
  - **Societal differences**

What are the regulations and policies we have to follow?

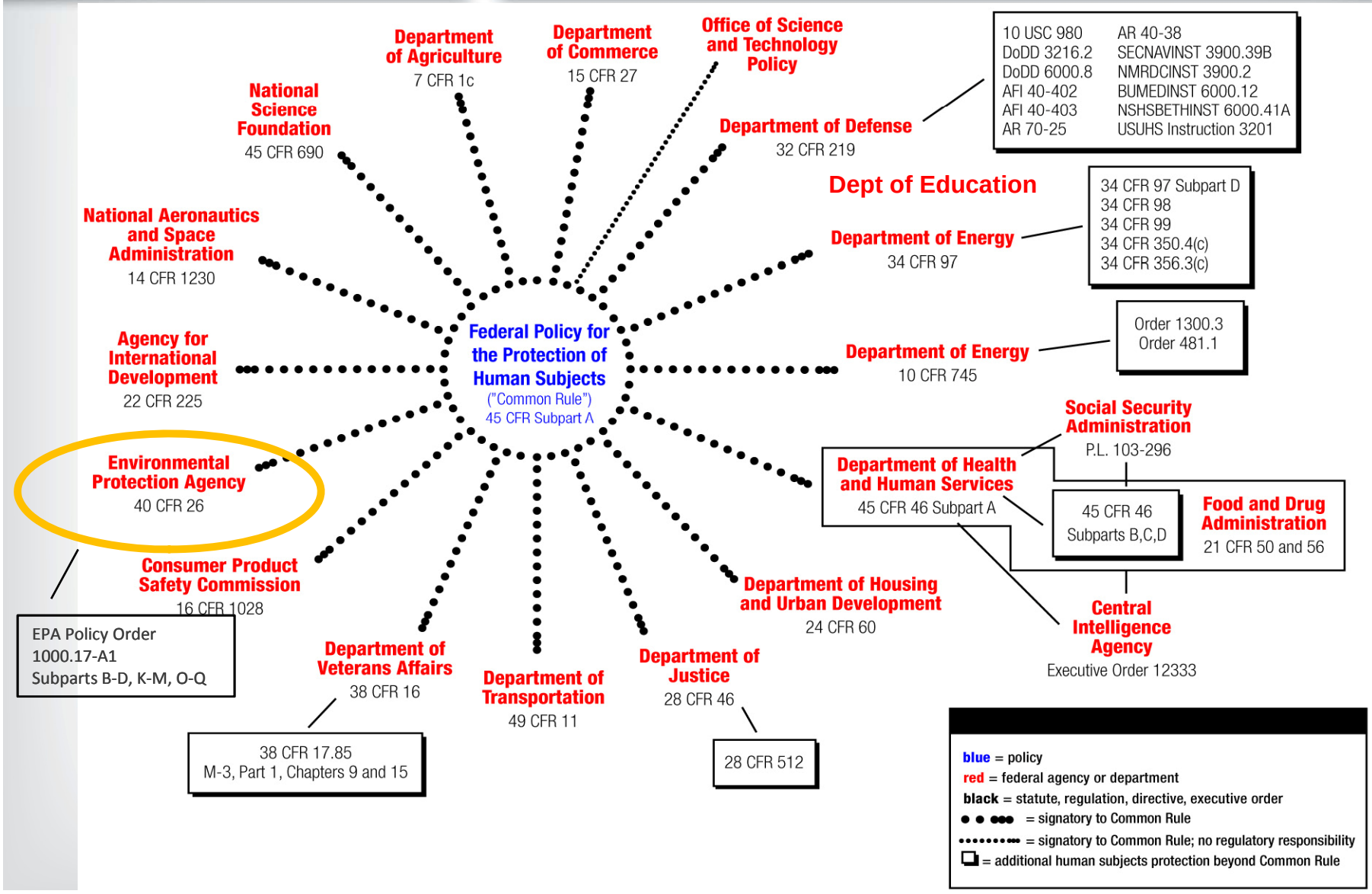
Translating Ethical Principles Into Regulations

Investigators and IRBs to note: Regulatory requirements stem directly from ethical principles

Federal Regulations Provide a "Patchwork Quilt" of Protections



Current Federal Regulatory Structure



Subpart A is "common"… but the other regulatory subparts are NOT

What's special about EPA's regulations?

- Subpart B: Prohibition of Intentional Exposure Research Conducted or Supported by EPA in Children and Pregnant or Nursing Women
- Subpart C: Additional Protections for Observational Research Conducted or Supported by EPA in Pregnant Women and Fetuses
- Subpart D: Additional Protections for Observational Research Conducted or Supported by EPA in Children

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- Subpart K: Regulation of Third-Party Intentional Exposure Research for Pesticides in Non-Pregnant, Non-Nursing Adults
  - Subpart L: Prohibition of Third-Party Intentional Exposure Research for Pesticides in Children and Pregnant or Nursing Women
  - Subparts M-Q: Regulations for reviews of proposed and completed research

EPA vs. HHS: Regulatory Restrictions

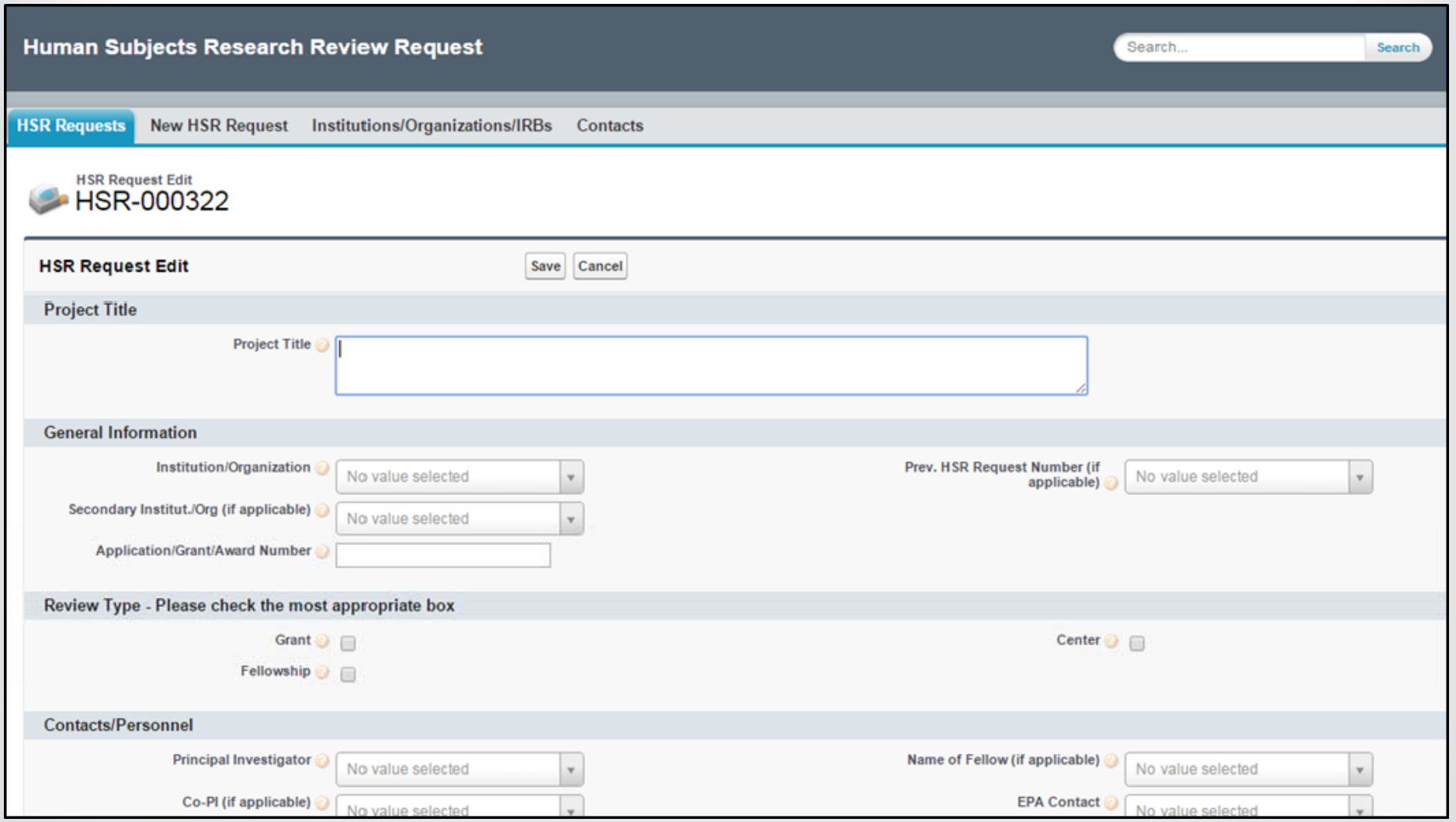
EPA	HHS
PREGNANT or NURSING WOMEN	
Categorical ban on intentional exposure research	No such categorical ban
No mechanism for research "not otherwise approvable"	Research "not otherwise approvable" may be conducted under special circumstances
CHILDREN	
Categorical ban on intentional exposure research	No such categorical ban
No mechanism for greater than minimal risk research without prospect of direct benefit	Mechanism exits (406)
No mechanism for research "not otherwise approvable"	Research "not otherwise approvable" may be conducted under special circumstances (407)

IRB Variations

- **Each IRB functions in a fairly distinct method:**
  - **Expectations for the PI:**
    - **Anticipation and minimization of culturally-specific risks**
    - **Cultural Context Letters**
    - **Translated consents (if in non-English speaking community)**
    - **FWA for studies in foreign locales**
    - **Certificates of Confidentiality**

- **Non-familiarity with EPA studies**
  - **Institution specific (everyone except UNC-Chapel Hill!)**
  - **PI as advocate for research**
  - **Types of review related to level of risk**

HSRRO Review Request



Human Subjects Review for NCER (grants and fellowships)

Final approval for studies involving human subjects, database studies, and substantive changes in approved studies

Conditional Approval of studies involving human subjects

Minor changes to approved studies; studies that do not qualify as human subjects research

Not human subjects research