Human Research Protection Program (HRPP) Reaccreditation

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Objectives

- This session provides an overview with questions related to IRB Domain II (27 Elements)
- Your objective is to Participate
- Should you wish to explore any topic in more detail by accessing the slide handout & IRB Q and A Guide on the ORI AAHRPP webpage.

AAHRPP REVIEW

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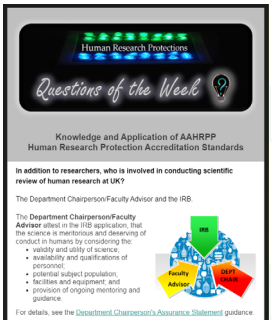
How do you learn about AAHRPP?



Training Materials
Training materials to help you prepare
Learn More

Training Sessions
Dates/Times/Locations
Learn More

Questions of the Week
Questions that may be asked
Learn More

Updated Policies
Changes in policies
Learn More

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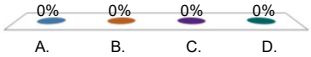
Who serves as the Institutional Official (IO) for the UK HRPP?

A. ORI Director
B. IRB Executive Chair
C. Vice President for Research
D. University President



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Ethical & Regulatory Framework

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What Ethical Principles do you follow?

8

Ethical Principles *Belmont*

Respect for Persons

individual treated as autonomous agent and those with diminished autonomy (vulnerable) are entitled to protection

Beneficence

minimize harm; maximize benefits and well being. Obligations of beneficence apply to individuals and society as a whole

Justice

fair distribution of benefit and risks. No one group disproportionately receive benefit or bear burden

What issues does IRB consider in review of Comparative Effectiveness Research?

Randomized Challenge of 2 or more SOC Therapies

1. Respect
2. Beneficence – Risk – Benefit
   - How can risk be minimized?
   - Is risk reasonable relative to potential benefit ?
3. Justice

Comparative Effectiveness Research?

Randomized Challenge of 2 or more SOC Therapies

An investigator wants to conduct a challenge study comparing two FDA-approved hypertensive drugs in a randomized, controlled trial including adults 18-80 years of age with essential hypertension.

Both are commonly used, standard-of-care treatments.

While the literature doesn't demonstrate one product to be superior, it is documented that drug B is more effective than drug A in adults older than 50.

IRB questions/considerations?

Respect for Persons

Informed Consent PROCESS
Withdraw Procedures

Beneficence

Risk – Benefit
Study Design
Safeguards

Justice

Representative Population
Fair Recruitment Practices

What Rules do You Follow?

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Regulatory Layers

- Law
- UK Policy
- Funding agency
- Regulations (FDA, HIPAA)
- *DHHS Federal Policy for Protection Human Subjects- "Common Rule"*

& Vulnerable Subject Sub-Parts

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Revised Common Rule Regulation

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In January 2019, UK ORI transitioned existing studies to the revised common rule

A. True
B. False

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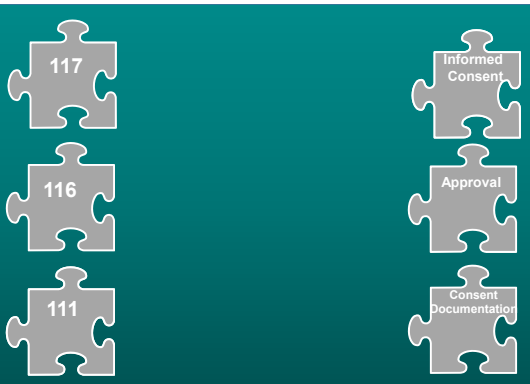
Common Rule Citations vs Terms



IRB Regulatory Checklists

- Criteria for Approval & Consent [PDF]
- Continuation Review Primary Review [PDF]
- Expedited [PDF] & Exempt Reviewer [PDF]
- Department of Defense [PDF]
- Emergency Use [PDF]
- PI Department of Energy [PDF]
- Department of Education [PDF]
- Environmental Protection Agency [PDF]
- Department of Justice [PDF]
- HIPAA [PDF]

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Element I.1.E. Education

Name education resources or training and opportunities provided to IRB members.

Element II.1.B & II.1.E

- The membership of the IRB or EC must be qualified through the experience and expertise, or the use of consultants.
- Give example of consultation

Element II.1.D

- IRB members must not participate in the review of any protocol in which they have a conflict of interest, except to provide information requested by the IRB

Conflict of Interest (COI)

- set of circumstances that creates a risk that one's professional judgment or actions regarding a primary interest (e.g., the integrity of research, the welfare of human research subjects) will be unduly influenced by a secondary interest (e.g., financial gain, other personal interest).



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If Research Related SFI cannot be eliminated..

COI MGT Plan → RCOIC Review → VPR Approval → IRB Review

- Investigator works with Office of Sponsored Projects (OSPA) on Management Plan
- Reviewed by Research Conflict of Interest Committee (RCOIC)
- Vice President for Research (VPR) – Institutional Official final approval, monitoring compliance and reporting to sponsoring agency
- Institutional Review Board (IRB) – subsequent review; IRB may not change the approved plan, but, it may impose further restrictions/conditions on the protocol or disapprove the protocol.

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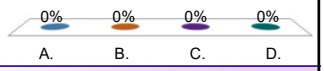
Who has final say in determining whether research with a S-COI may be conducted?

A. RCOIC
B. VPR
C. IRB
D. OSPA



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What activities need IRB Review?

Who provides an official determination whether an activity needs IRB review?

IRB Chair, Designee, ORI Director, ORI Associate Director

Upon what is the determination based?

Common Rule Definition of Research & Human Subject
FDA Definitions Human Subject & Clinical Investigation n=1
IRB Standard Operating Procedures
OHRP Guidance (2008 guidance for coded info/specimen)
OHRP Engagement Memo
DoD Definition of Experimental Subject

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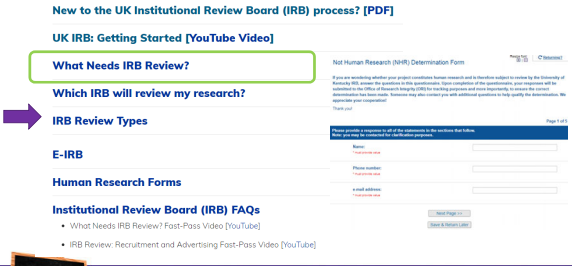
ORI Getting Started Website

www.research.uky.edu/office-research-integrity/getting-started



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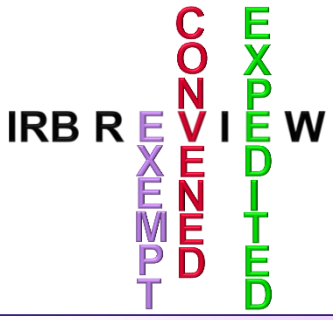
Standard II.2.A



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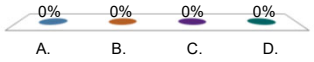
Who makes Exempt determinations?

A. Investigator
B. An IRB member
C. Any member of ORI Exempt Dream Team
D. The Exempt IRB Committee



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What's new with EXEMPT Review?

- New & Revised Categories
- Category 2 & 3 (7,8) require Limited Review
- Some overlap with existing Expedited Categories
- If you don't know answer, say you would refer to:
  - Exempt Tool (Table)
  - Exempt Category Flow Charts
  - ORI Dream Team

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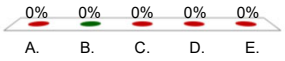
Limited IRB review considers…

A. 111 criteria for approval
B. Prospective agreement
C. Minimal Risk
D. Privacy & Confidentiality
E. None of the above



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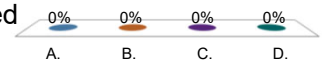
UK conducts Annual Administrative Review (AAR) for which Expedited Protocols?

A. Pre-2019
B. Non FDA-Regulated
C. Post-2019
FDA-Regulated
D. Post-2019
Non FDA-Regulated



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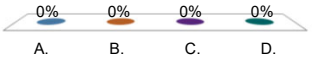
Who has authority to approve major revisions for a Convened IRB review?

A. ORI Staff
B. IRB Chair
C. Convened IRB
D. Designated IRB Member



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The IRB agenda for Convened meetings advises the IRB of research studies approved using expedited review procedures. Any member can request to review IRB an expedited study submission.

A. True
B. False

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Give an example of a controverted issue from a Convened meeting.

- Controverted issues are those that cause controversy and dispute among the IRB membership.
- The minutes must summarize
  1. The IRB's discussion
  2. The Resolution

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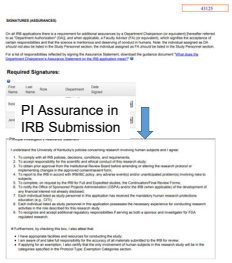
How does IRB inform investigators regarding roles and responsibilities?



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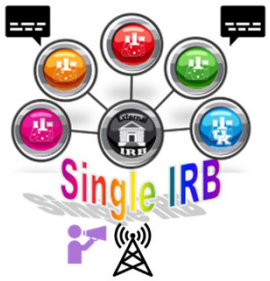
www.research.uky.edu/office-research-integrity/researchers

What's new in IRB Reliance?



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Transition to Single-IRB

- NIH policy January 2018- *same NIH-funded protocol at multiple sites*.
- Revised Common Rule January 2020- *most federally-funded collaborative research – 2 or more institutions.*

ORI Reliance
www.research.uky.edu/office-research-integrity/single-irb-reliance

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Authorization Agreement

- describes the respective authorities, roles, responsibilities, and communications between an institution providing IRB review and participating site relying on the IRB.

Ceded protocols – External IRB

Investigator:

1. submits Reliance Registration/Request Form
2. creates E-IRB Abbreviated Application
   - Tracking to direct subjects or staff to correct contacts
   - Prompts PI on local ancillary processes that may need completion (e.g., HIPAA, COI, Investigational Drug Service, Biosafety review).

Criteria for IRB Approval

("Common Rule Regulation" 45 CFR 46.111)

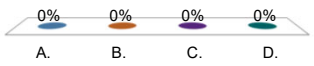
☑Risks are reasonable in relation to anticipated benefits.
☑Risks to subjects are minimized.
☑Confidentiality is maintained.
☑Privacy is protected.
☑Selection of subjects is equitable.
☑Additional safeguards are included for vulnerable populations.
☑Data collection is monitored to ensure subject safety.
☑Informed consent is sought from each subject.
☑Informed consent is appropriately documented.

Study Design & Safeguards to Minimize RISKS

- Utilize procedures already being conducted
- Screening to rule out "at risk" subjects
- Professional Counseling Services
- Increased oversight
- Data security measures
- Create stopping rules
- Choose least intrusive design that yields valid data
  (e.g., Sequential Multiple Assignment Randomized Trial or SMART trail)
- Certificate of Confidentiality for legal risks

You question the proposed setting for approaching potential participants, you are considering…

- A. Privacy
- B. Data
- C. Confidentiality
- D. Transparency



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Confidentiality & Privacy

Data & how it is Protected

How data will be maintained, stored, transferred, etc.

People & their Expectations

Individual concept shaped by situation, experience, values, culture, beliefs, etc.

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RECRUITMENT METHODS

- **Equitable Selection** –

Proportionate Distribution; not targeting or excluding based on convenience

- **Undue Influence** –

No finders fees or recruitment bonus to study staff; appropriate IRB-approved ads; 3rd party if PI is an authority figure

- **No Cold Contacts** –

contact by personnel with legitimate access or through individuals with established relationships

- **Compensation** –

appropriate amount, method, and timing

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PI Guide to Identification & Recruitment of Human Subjects for Research

Populations with special regulatory or institutional protections

- ❑Children
- ❑Prisoners
- ❑Pregnant\Fetus\Neonate
- ❑Adults with Impaired Consent Capacity
- ❑K-12 Students
- ❑University Students
- ❑Non-English Speaking
- ❑Economically or Educationally Disadvantaged

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IRB Review of Consent DOCUMENT & PROCESS

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The Revised Common Rule General Consent Requirements reference which of the following:

A. Reasonable Person
B. Concise & Focused
C. Sufficient Detail
D. A & B
E. A, B, & C

0% 0% 0% 0% 0%
A. B. C. D. E.

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How do you evaluate if proposed consent meets General Requirements, such as:

- Understandable language
- Occurs before involving participant
- Provides sufficient time to consider
- Concise, focused, sufficient detail
- Meets the reasonable person standard
- Facilitates comprehension

Document & Process

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PROCESS is described in the Research Description

- Who:
  - PI may delegate to authorized personnel but ultimately responsible
- How:
  - Minimize coercion, undue influence, therapeutic misconception
  - Use of visuals, aids, verbal concepts, demos, or learning tools
  - Methods to assess understanding
- When:
  - Ample time for participant
  - Prior to research activity
  - Ongoing throughout
  - Key Information FIRST

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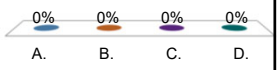
Key Information

A. Is best practice but not regulation
B. Includes main inclusion and exclusion criteria
C. Includes required elements of informed consent
D. Includes the main reason(s) to be & not to be in a study



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Key Information

- It is a Post 2019 regulatory requirement for the PROCESS & FORM [unless sufficiently short]
- *"It gives potential subjects the bottom line first".*
- *"It's the movie trailer version of the research".*

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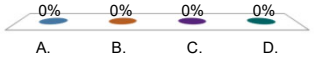
Informed consent documents must:

A. Include required regulatory elements
B. Follow the UK consent template
C. Be signed by the PI
D. All of the above



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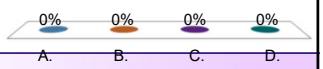
Which of the following UK IRB templates is a valid informed consent document?

A. Debriefing & Permission to Use Data Form
B. Cover Letter Template
C. Assent Form
D. HIPAA Authorization Form



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Cover Letter

- even though it sounds like something attached to a resume…for IRB purposes,
  - "Cover Letter" refers to a type of consent document with a concise presentation of the required elements of consent, and is often used at the beginning of research surveys.
- Valid consent, but for minimal risk survey done online or on phone, requires IRB Waiver of Documentation

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Waiver of Consent Documentation

requires an oral or written process to include all required applicable elements of consent.

What is waived?

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Waiver of Documentation Options

(i) Option 1- Consent ONLY linked record and Principal Risk is Breach of Confidentiality Form

(i) Option 2-<Minimal Risk & procedure where written consent not norm outside of research – *USE Cover Letter Template*

(i) Option 3- <Minimal Risk & Distinct Cultural Group Community in Which Signing Form is Not the Norm

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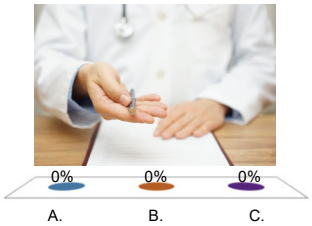
Under which waiver of documentation option, must the consenting subject be asked whether she/he wants to sign a consent document?

A. 1- principal risk breach of confidentiality
B. 2 – minimal risk for which consent not required outside of research context
C. 3 – culture in which signing forms is not the norm



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What regulatory determination does IRB consider for a request to withhold the study purpose until after data collection?

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What Criteria does IRB consider for request to WAIVE OR ALTER informed consent?

1. The Research Presents No More than Minimal Risk;
2. Research Could Not Practicably be Conducted without the Requested Waiver or Alteration;
3. If Using Identifiable Private Information or Identifiable Biospecimens, Research Could Not Practicably be Carried Out without Using Such Information or Biospecimens in an Identifiable Format;
4. Waiver or Alteration Will Not Adversely Affect Rights & Welfare of Subjects;
5. Whenever Appropriate, the Subjects or Legally Authorized Representatives Will be Provided with Additional Pertinent Information After Participation.

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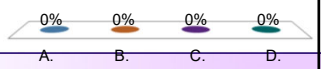
What do Common Rule regulations state about Re-consent?

A. Nothing
B. It must occur at least annually
C. It should include active participants
D. It must occur when any new information is available



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Federal common rule does not reference the term "re-consent."

…when appropriate, participants will be provided with significant new findings that develop during the research which may relate to their willingness to continue participation
(45 CFR 46.116(c)(5)).

www.research.uky.edu/uploads/ori-d1000000-would-you-ever-need-re-consent-research-participant-pdf

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All UK human subject research must include a Data & Safety Monitoring Plan (DSMP)

A. True

B. False

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Data & Safety Monitoring (DSMP)

UK IRB requires a Data and Safety Monitoring Plan (DSMP) for:

- ***Greater than minimal risk research***
- ***NIH Funded Clinical Trial***
- ***FDA Regulated Clinical Investigation***

The ORI website provides guidance for developing a Plan- www.research.uky.edu/office-research-integrity/resources-data-and-safety-monitoring

Some plans include Data Safety Monitoring Boards (DSMB)

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Ongoing IRB Oversight Investigator Reports & Requests

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Violations, Prompt Unanticipated Problems, Non-Compliance

Primary Reviewer

- MAJOR Violation;
- Suspected NC; or
- Prompt UP

Full IRB Review

- Need more info
- Consider risks to subjects (action or inform) or
- Investigator Corrective Action

Acknowledge - No additional action

OR

Regulatory Determinations

Serious Non-Compliance

Continuing Non-Compliance

UP Involving Risks to Subjects or Others

Suspension

Termination

If YES,
Mandatory Reporting to:

- Regulatory Agency
- Funding Organization
- AAHRPP
- UK Official

What does ORI/IRB Promptly Report to AAHRPP?

- Any negative actions taken by a government oversight office (OHRP Determination Letters, FDA Warning Letters or restrictions);
- Any lawsuits (i.e., litigation, arbitration, or settlements initiated) related to human subject research protections; or

- Press coverage (TV, newspaper, online publications) of negative nature regarding the UK HRPP.

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FDA research regulations apply to studies evaluating only products that require FDA marketing approval.

A. True

B. False

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Marketing Regs ≠ Research Regs

- If research involves testing or assessment of articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease . . .” and “articles (other than food) intended to affect the structure or function of the body...” treat as FDA-Regulated Study

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IRB Responsibilities for FDA Regulated Research

If protocol involves testing or collecting data on a specific FDA-regulated product, the IRB must:

1. Assure Qualifications of Investigators
2. Assess Adequacy of Research Sites
3. Question if an Investigational New Drug (IND) or Investigational Device Exemption (IDE) is required and on what basis of the sponsor’s determination.

August 2013 FDA guidance – IRB Responsibilities
www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM328855.pdf

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