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Rapid Fire Training Plan

- This session provides an overview with questions related to the 62 elements across 16 standards.
- Designed for broad audience, accordingly, some information will not applicable for all studies. Consider concepts within context of your research.
- Participate
- Explore any topic in more detail by accessing the slide handout and Investigator Q and A Guide on the ORI AAHRPP webpage.

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3

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Ready?

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4

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Human Research Protection Program (HRPP)?

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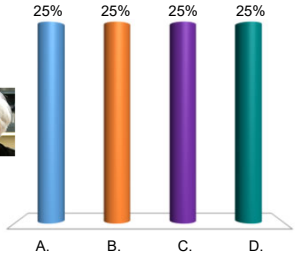
Who serves as the Institutional Official (IO) for the UK HRPP?

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



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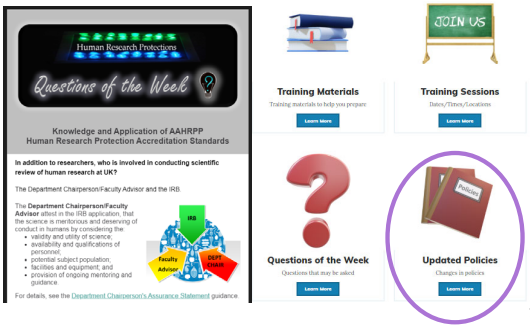
How do you learn about….



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Who can you contact with Questions, Suggestions, Concerns?

- ORI Administration or Subject Rights: Helene Lake-Bullock, ORI Director (1-866-400-9426/ 257-9428 / hlbullo@uky.edu)
- ORI anonymous online customer feedback form https://redcap.uky.edu/redcap/surveys/?s=jB2Nfm
- IRB Chair; appeal process

8

8

Office Hours & Consult Requests

Office of Research Integrity (ORI) Office Hours

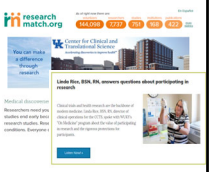
Meet with ORI staff in an informal setting and get immediate feedback and advice on any IRB-related questions.

9

9

What resources and contacts are available for the public and participants?

- The CCTS Participant Website and ORI Participant Website provides participant education links, event notices, research opportunities, and contact information.
- Every consent document includes PI and ORI contact information > minimal risk research 24/7



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Ethical & Regulatory Framework

11

11

What Ethical Principles do you follow?

12

12

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

13

Ethical Principles *Belmont*

Respect for Persons

Informed Consent
Privacy Respected
Clear Withdraw Procedures

Beneficence

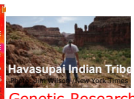
Study Design
Safeguards
Stopping Points

Justice

Representative Population
Avoid Undue Exclusion
Fair Recruitment Practices

14

Modern Day Ethical Issues –



Genetic Research

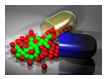
PhotoVoice

Internet & Social Network Research

Comparative Effectiveness Research

Biospecimens

Big DATA



Transparency Pharma/FDA

15

How would you reduce risks in Comparative Effectiveness Research?

A sponsor wants to conduct a challenge study comparing two FDA-approved hypertensive drugs in a randomized, controlled trial including adults 18-75 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 60.

16

Consider ethical principles:

Education researcher evaluating how background noise affects student's ability to concentrate. To evaluate, she will have students complete an assignment, however she requests to withhold the purpose of the research as it would bias results.

Beneficence

Respect

Justice

17

17

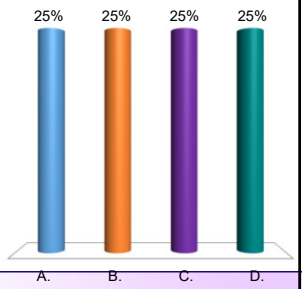
What Rules do You Follow?

18

18

What IRB Regulation is applied to every UK human research study?

A. Food & Drug Administration (FDA)
B. Health & Human Services (DHHS) Common Rule
C. National Institutes of Health (NIH)
D. AAHRPP IRB Regulations



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19

Regulatory Layers

State Law
Institutional Policy
Funding agency requirements (DoD, NIH)
Additional Regulations (FDA, HIPAA, FERPA)
Department of Health & Human Services (DHHS)
Federal Policy for Protection Human Subjects-
"Common Rule" & Vulnerable Subject
Sub-Parts (e.g., children, prisoners)

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20

Revised Common Rule Regulation

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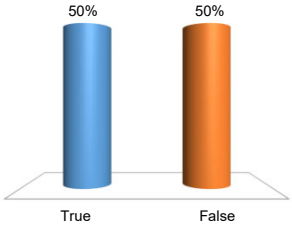
21

21

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

A. True
B. False



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23

How do you determine what activities need IRB Review?

= IRB Review

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24

Common Rule Definition of Research & Human Subject?

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

Human Subject –
a living individual about whom an investigator conducting research:
Obtains, uses, analyzes identifiable information (or specimens) through intervention or interaction with the individual, or their identifiable private information.

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Research or Not-Research

Examining retrospective and prospective medical records to compare the effectiveness of two different treatments

Using patient surveys and medical records to create a locally applicable rating system for medical providers

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Nancy McGill

26

Human Subject or Not Human Subject

Medical Record Review
Decedent data
A person completing a marketing survey
Leftover blood from your clinical trial subject
De-identified specimens from an Honest Broker

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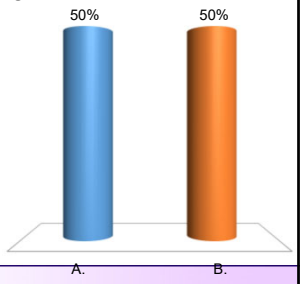
If I can see your private information, but I promise not to record any identifiers when collecting research data, the activity is not human subject research.

A. True
B. False



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28

- can see the identifiers
- have key to a code
- have treatment relationship
- can readily connect dots
- record

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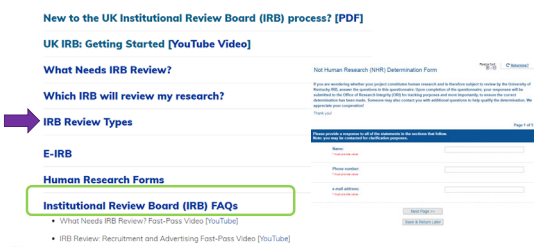
ORI Getting Started Website

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



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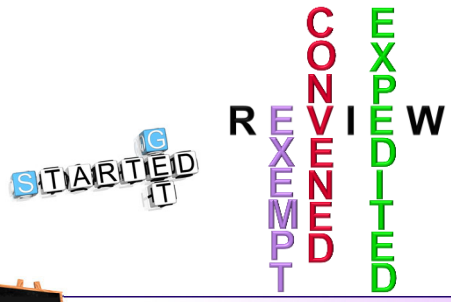
3 Initial Review Types



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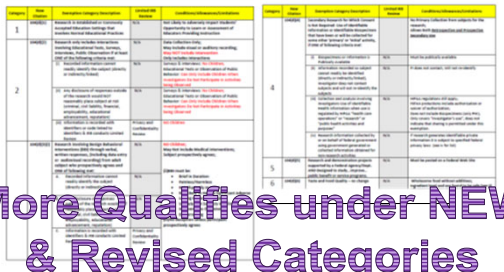
31

What's new with EXEMPT Review?



More Qualifies under NEW & Revised Categories

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What's New with Expedited Review?

- Revised Rule no longer required Continuing Review for Post 2019 Expedited
- Non-FDA Regulated Expedited research will undergo an Annual Administrative Review (AAR) instead of a Continuing Review (CR)

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What's new in IRB Reliance?

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34

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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35

Authorization Agreement

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

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36

36

Ceded protocols – External IRB

PI:

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).

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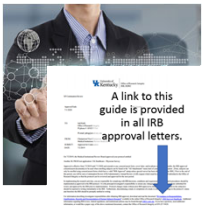
37

37

38

Investigator Role & Responsibilities

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



- IRB Compliance
- Resources
- Qualifications
- Informed Consent Process & Documentation
- Monitoring & Oversight
- Records & Documentation
- Responsibilities for Research Reviewed by Non-UK IRB

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39

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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40

40

Researcher COI

- State statutes, Federal Reg, & UK Adm. Reg 7:2
- Who: Researchers & Immediate Family
- Disclosure: annually, within 30 days of new COI, each funding proposal or IRB application
- Significant financial interest (SFI): >$5000 interest, intellectual property, industry sponsored travel (*not salary, remuneration or government sponsored activities*)
- Unsure: Contact Emily Bradford, 257-9420 Office of Sponsored Projects Administration (OSPA)

41

41

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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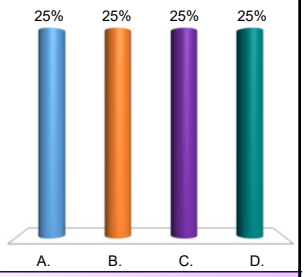
42

42

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

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



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Feasibility – Resources

- Ability to recruit in sufficient numbers
- Sufficient time to conduct study
- Adequate qualified staff
- Suitable facilities
- Appropriate task delegation
- Informed team (protocol, role)

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44

44

45

Qualifications & Oversight

Investigator experience, credentials, qualifications
Study staff training and qualifications
Evidence of investigator involvement
Protocol specific training & communication
Appropriate task delegation
Adequate supervision

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46

46

Appropriate Task Delegation

- Who on your team…
  - Obtains informed consent
  - determines if subjects meet inclusion/exclusion criteria
  - evaluates causality of adverse events and relationship to study participation

While tasks may be delegated, responsibility ultimately remains with the Principal Investigator

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47

47

Investigator Qualifications and Provision of Medical Oversight

Guidance on IRB & FDA expectations for qualifications, supervision, delegation, etc.
www.research.uky.edu/uploads/ori-d1280000-investigator-qualifications-and-provision-medical-oversight-pdf

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48

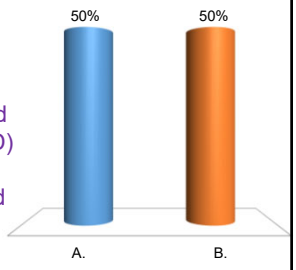
48

Do FDA regulations allow a non-physician investigator serve as PI of FDA-regulated research?

A. Yes

B. No

However, if PI is a non-physician, a qualified physician (MD, OD, DMD) should be listed as a sub-investigator & should be responsible for medical decisions.



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50

50

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

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51

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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52

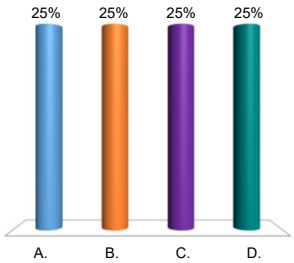
Considering the appropriate setting for approaching potential participants, protects..

A. Privacy

B. Data

C. Confidentiality

D. Transparency



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53

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

54

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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55

Educationally or Economically Disadvantaged, What safeguards do you consider?

Inclusion
Exploitation
Undue Influence
Balanced Compensation
Informed Consent
Guidance - www.research.uky.edu/uploads/ori-d1390000-research-involving-economically-or-educationally-disadvantaged-persons

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56

56

57

Informed Consent Document

- How do you evaluate whether a consent form …..
  - is understandable,
  - is concise, or
  - Provides Information that meets the reasonable person standard?

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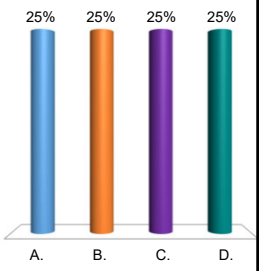
58

58

Key Information

A. Is best practice but not a research 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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59

Key Information

- It is the key reason(s) that would make the average person to say 'yes' and the key reason(s) that most people would choose as grounds for saying 'no'.
- *"It gives potential subjects the bottom line first".*
- *"It's the movie trailer version of the research".*
- It is a regulatory requirement for the FORM & PROCESS

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60

60

PROCESS is described in the Research Description

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

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61

61

Who is required to sign the informed consent document at UK?

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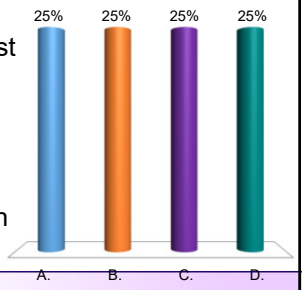
62

62

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)).

PI and IRB evaluate New Information

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64

64

Communicating New Information

See Reconsent Notification Guidance for Considerations and Criteria for Determining Communication Method/Process

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

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65

65

Informed Consent Waiver vs. Waiver of Documentation

- Under very select circumstances, regulations permit IRB to:
  1. waive/alter the informed consent (alter would involve omitting any one of required elements of informed consent); or
  2. waive documentation of informed consent.

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66

66

Consent Waiver Criteria:

(i) The Research No More than Minimal Risk;

(ii) Could not practicably do without Waiver or Alteration;

(iii) Could not practicably do without using Identifiable Private Information or Identifiable Biospecimens (if applicable);

(iv) Will Not Adversely Affect Rights & Welfare of Subjects; and

(v) Whenever Appropriate, will Provide Additional Pertinent Information After Participation.

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67

Waiver of Consent Documentation

Oral or written process must include all required applicable elements of consent.

What is waived is the _____ 

(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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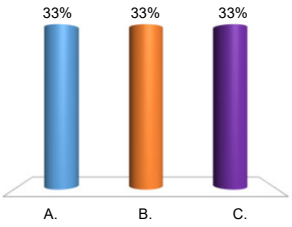
68

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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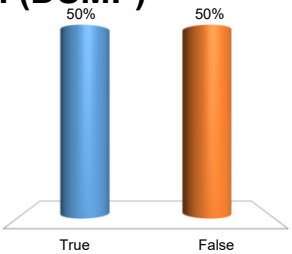
70

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

A. True

B. False



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71

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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72

72

Data & Safety Monitoring Boards (DSMB)

DSMB - an independent or external panel established by a sponsor to assess at specific intervals the progress of a clinical trial, safety data, and critical efficacy variables to recommend whether to continue, modify, or terminate a trial based on the panel's findings.

VIEWS AGGREGATE UNBLINDED DATA

Can identify trends and make meaningful recommendations

Submit DSMB reports or findings to IRB as available and at Continuing Review.

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74

74

Compliance with Protocol and Approved Research Description

Unless done to prevent immediate harm, proposed PROTOCOL changes must be reviewed by the IRB prior to implementation

- Modification Review

To request changes impacting single subjects, request a:

- Exception or Deviation

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75

75

Exceptions, Deviations, Violations

- Exceptions & Deviations – IRB approved

  - Exception – to approved enrollment criteria for 1 subject
  - Deviation – one-time deviation from approved protocol

- Protocol Violations (major or minor) – happened without IRB approval

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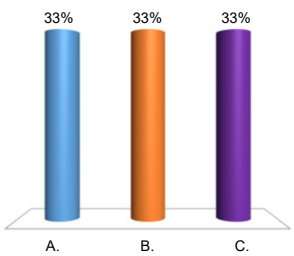
76

IRB request to obtain serum pregnancy test, when protocol only specified urine dipstick.

A. Protocol Exception
B. Protocol Deviation
C. Protocol Violation



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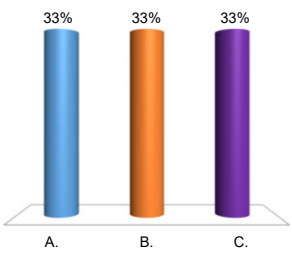
77

Request to enroll a 66 year old subject when inclusion criteria specifies 18-65 years of age.

A. Protocol Exception
B. Protocol Deviation
C. Protocol Violation



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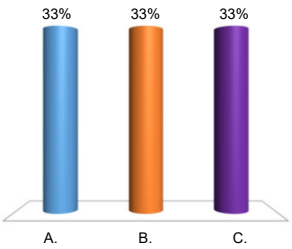
Failure to obtain informed consent until after initiation of study procedures.

A. Protocol Exception
B. Protocol Deviation
C. Protocol Violation



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79

Other IRB Reports

80

Adverse Event (AE) & Unanticipated Problem (UP)

- Follow sponsor requirements identifying, recording, managing, and reporting AE and UP –
- _____ responsible for determining causality
- Follow UK IRB safety reporting requirements – Prompt & Non-Prompt

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81

Promptly Report Unanticipated problem involving risks to subjects or others (UPIRSO)-

Includes any incident, experience, or outcome that meets **all:**

1. Unexpected;
2. Related or possibly related to participation in Research; and
3. **Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.**

higher threshold in that involves risks to subjects or others and alters the risk-benefit ratio

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82

Other PROMPT reports

- Unanticipated adverse device effect resulting in harm
- All Research-Related Deaths (expected or unexpected)
- Other Events in PI's judgement, warrants reporting
- Other events that impact the conduct or integrity of the study:
  - FDA clinical hold or recall, Inspection, Litigation, or Press involving Human Subject Protection
  - Investigator medical licenses suspension
  - Subject incarcerated

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83

84

84

When do Food & Drug Administration RESEARCH Regulations apply?

- Studies that collect data on products that meet the FDA definition of Drug, Device, or Biologic.
  - IRB 21 CFR 56
  - Informed Consent 21 CFR 50
  - Investigational Drug/Biologic 21 CFR 312
  - Investigational Device 21 CFR 812

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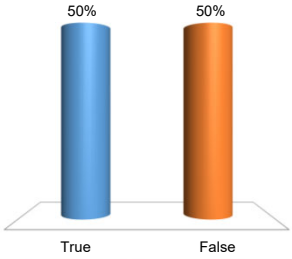
85

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

A. True
B. False



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86

86

Marketing Regs ≠ Research Regs

- FDA regulations may apply to products that do not need FDA approval for marketing.
- If research involves 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...”

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87

FDA Warning Letter

"Maxey Cosmetics (M-Cosmetics) will use volunteers to test an eyelash growth-enhancing product.... " This statement regarding eyelash growth makes clear that this product is intended to affect the structure or function of the body of man or other animals and therefore causes your product to be subject to regulation as a drug.

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88

IRB Submission

- Complete the Drug/Device Section
- Attached Drug/Device Form
- Attach indications/labeling/manufacture information, FDA correspondence, to provide the IRB with the information needed to make the required assessments.

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89

FDA delegated IRB Responsibilities

1. Ensure appropriate Qualifications
2. Assess adequacy of Facility (including accountability, storage, dispensing, etc.)
3. Does study need to be conducted under an FDA Investigational New Drug (IND) or Investigational Device Exemption (IDE) application?

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90

IND & *IDE* Categories

- Drug study:
  1. Exempt from IND requirements
  2. Requires IND Submission to FDA
- Device study:
  1. Exempt from IDE requirements
  2. Significant Risk Device – subject to FULL IDE requirements; IDE submission to FDA
  3. Nonsignificant Risk Device - "ABBREVIATED IDE" requirements; conducted under purview of IRB

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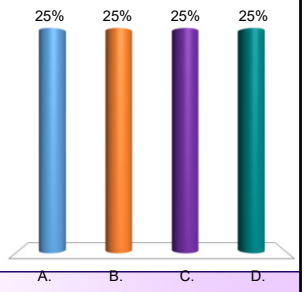
91

Research examining the safety or effectiveness of a medical device must have an IDE, unless the…

A. study is Exempt from IDE Requirements
B. study includes a Significant Risk Device
C. device is a Class II Medical Device
D. device is diagnostic and not therapeutic



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92

92

FDA Sponsor & Investigator Responsibilities

Survival Handbook Investigator/Research Staff Responsibilities

- Investigator Responsibilities
- Investigator Qualifications
- Provision of Medical Oversight & Delegation
- Regulatory Requirements Sponsor-Investigators

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93

93

ORI IRB Survival Handbook

https://www.research.uky.edu/office-research-integrity/irb-survival-handbook

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94

94

95

95

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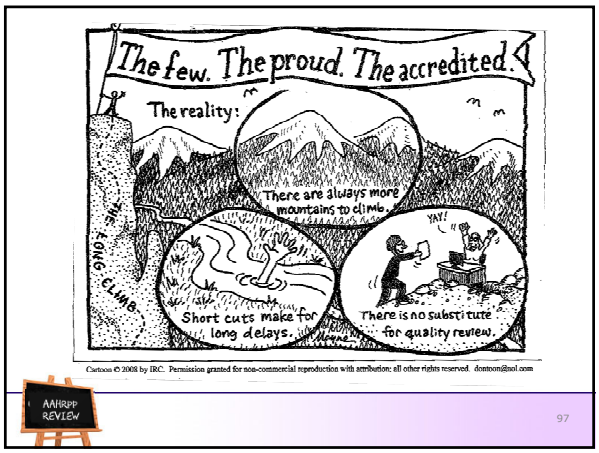
96

96


The few. The proud. The accredited.
The reality:
There are always more mountains to climb.
THE LONG CLIMB
Short cuts make for long delays.
YAY!
There is no substitute for quality review.
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97

97