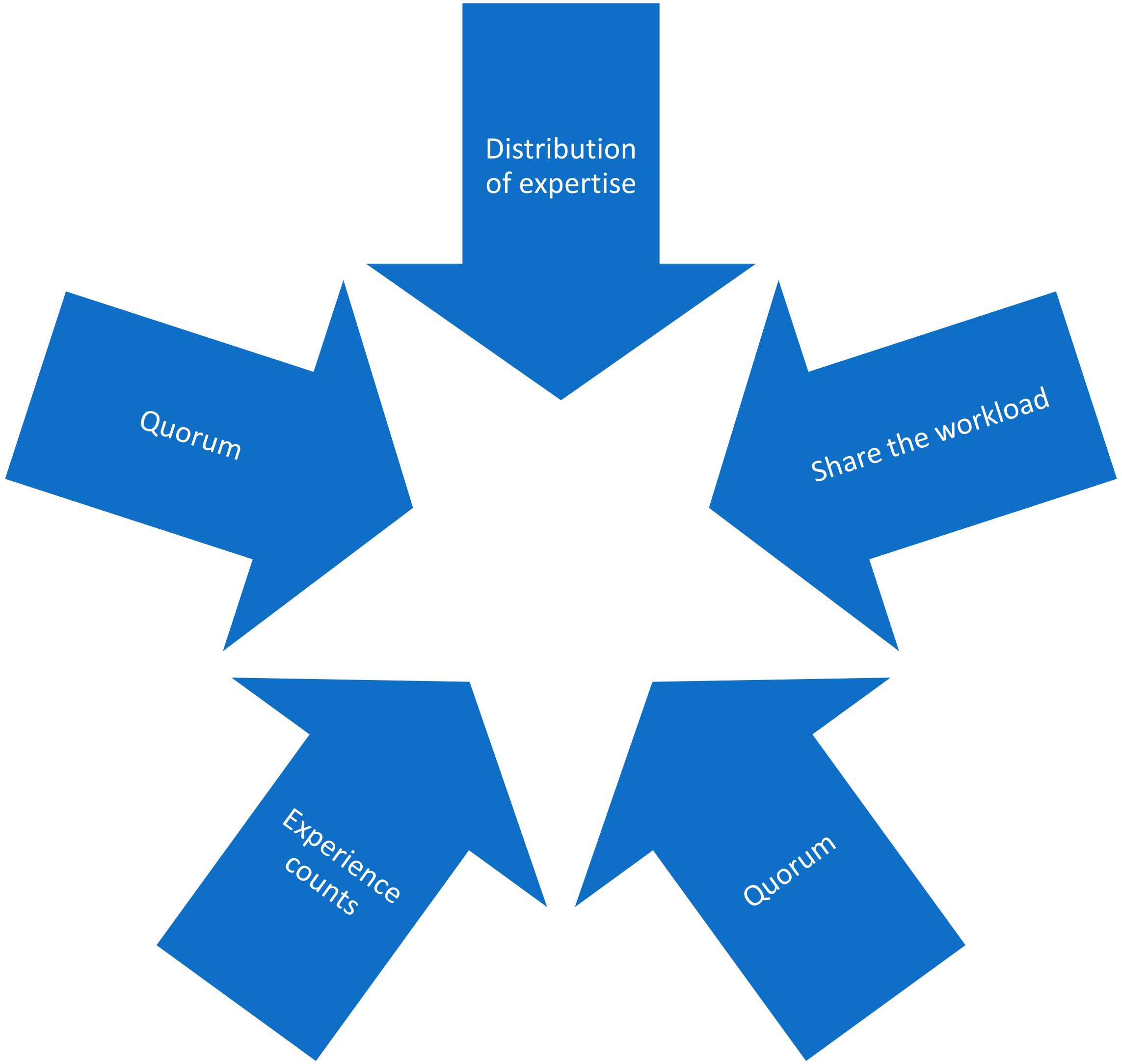
New IRB Member Training

NICOLE GRANT

Introduction

All meetings are held via Teams

Using NIH PROTECT electronic system



Distribution of expertise

Quorum

Share the workload

Experience counts

Quorum

Your commitment is important

The purpose of the IRB

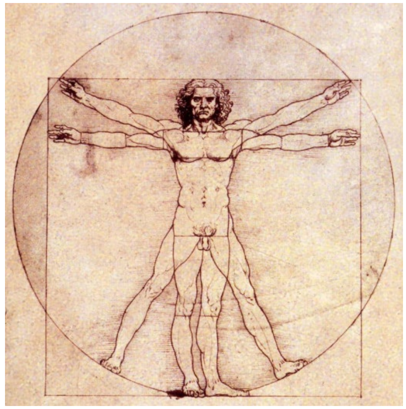
Ensure	Ensure the ethical conduct of human subjects research (45 CFR 46)
Protect	Protect the rights and welfare of participants
Certify	Certify that federal and institutional requirements for HSR are met

Definition of Human Subjects Research

PRE-2018 COMMON RULE

Human Subject means a living individual about whom an investigator (whether professional or student) conducting research obtains

- 1) Data through intervention or interaction with the individual, OR
- 2) Identifiable private information.



2018 COMMON RULE

Human Subject means a living individual about whom an investigator (whether professional or student) conducting research obtains

- 1) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
- (2) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

Definition of Minimal Risk

During all IRB reviews, we must determine the risk level

- Minimal risk
- Greater than minimal risk

Regulatory definition of Minimal Risk:

- that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests *(of healthy children living in a safe environment with prudent parents)*."
  - *"The standard of minimal risk should be interpreted as those risks encountered in the daily life of normal, average, healthy children living in safe environments and indexed to the experiences of children of the same age and developmental stage as the subject population"(FDA)*

From Belmont
to
45 CFR 46.111

THE CRITERIA FOR APPROVAL AND IRB REVIEW OF HUMAN SUBJECTS RESEARCH

“Scientific research has produced substantial social benefits. It has also posed some troubling ethical questions.”

  - The Belmont Report

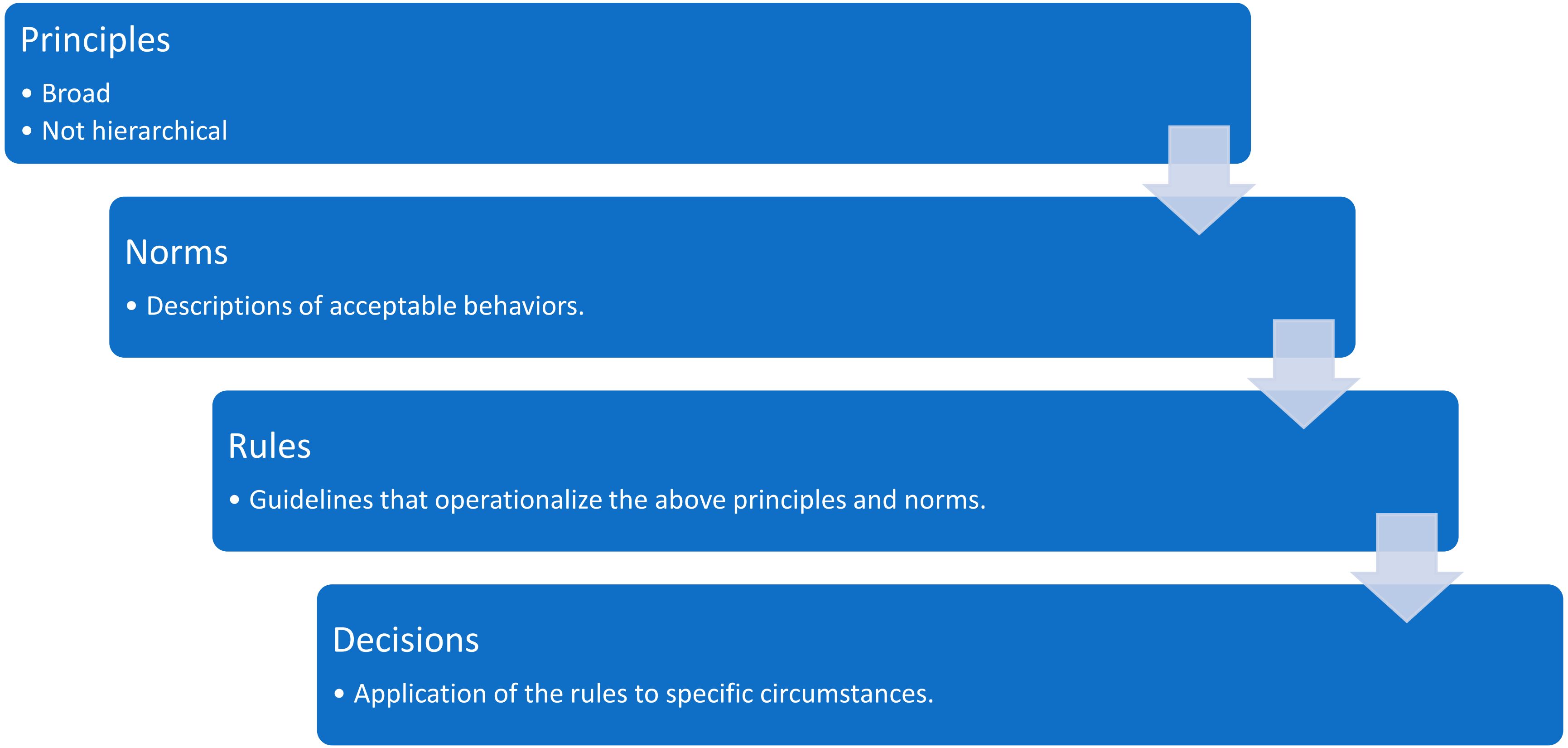
Your mission……

The central task of the IRB is to determine that the proposed research meets the criteria for approval as delineated in the Federal Regulations (45 CFR 46.111).

- In doing so, the IRB assures that the proposed research is ethical.
- Fulfillment of the criteria is both necessary and sufficient to judge a study ethical and approvable.
- It is exceedingly rare that unethical research would meet the criteria for approval.

IMPOSSIBLE

From principles to review



Principles

- Broad
- Not hierarchical

Norms

- Descriptions of acceptable behaviors.

Rules

- Guidelines that operationalize the above principles and norms.

Decisions

- Application of the rules to specific circumstances.

The Principles

Respect for Persons

Beneficence

Justice

No one trumps the other!

Respect for Persons

Principle

- “So act as to treat humanity, whether in thine own person or in that of any other, in every case as an end withal, never as a means only.”- Kant

Norms

- People should be treated as autonomous agents.
    - “individual capable of deliberation about personal goals and of acting under the direction of such deliberation”-Belmont Report
- Individuals with diminished autonomy are entitled to protection.

Respect for Persons: Criteria for approval

Informed consent

- (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, in accordance with, and to the extent required by §46.117.

Privacy/confidentiality

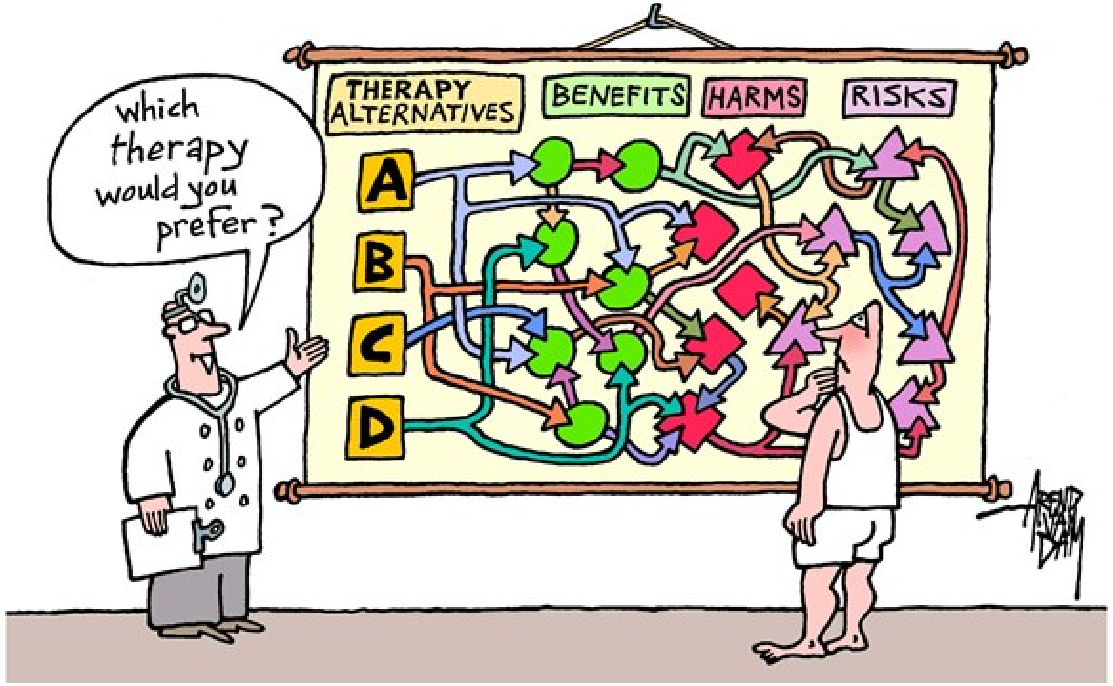
- (7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

Voluntariness and special protections

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

The transformative power of consent

CONSENT MAKES THE IMPERMISSIBLE PERMISSIBLE



Informed consent is not just the document

Process of consent

- Begins with the first contact with the potential participant and ends……?

Informed consent requires:

- Information
- Comprehension
- Voluntariness

Purpose of Informed Consent

- Purpose is to provide the information that people need to make an informed decision about whether or not to participate in the research
  - ➢ This information helps the individual determine if the research is consistent with their own goals and values
- The document is a basis for a meaningful exchange between the investigator and the subject
- Builds trust with the researcher
- Thorough understanding may also enhance subject safety during the research

Three Key Elements in the Informed Consent Process

Disclose information	disclose information to potential research subjects needed to make an informed decision
Facilitate understanding	facilitate the understanding of what has been disclosed
Promote voluntariness	promote voluntariness of the decision about whether to participate in the research under conditions free of coercion and undue influence

Is Information in the Consent Document Communicated Effectively?

- Some of the changes in the Revised Common Rule (2018) related to informed consent were intended to improve the presentation of material in the consent form
- Stemmed from concerns within the research community that consents had become too lengthy and complex
- Among other items, the 2018 Rule added 2 requirements for consent forms included in studies that receive initial approval on and after January 21, 2019
  - ➢ **A <u>key information section</u>** must be included at the beginning of the consent form
  - ➢ Information must be presented based on the **<u>reasonable person standard</u>**

Informed Consent—required elements

- A statement that the study involves **research**
- An explanation of the **purposes of the research**
- The expected **duration** of the subject's participation
- A description of the **procedures** to be followed
- Identification of any procedures which are **experimental**
- A description of any **reasonably foreseeable risks or discomforts** to the subject
- A description of any **benefits** to the subject or to others which may reasonably be expected from the research
- A disclosure of appropriate **alternative procedures** or courses of treatment, if any, that might be advantageous to the subject

Informed Consent—required elements

- A statement describing the extent, if any, to which **confidentiality** of records identifying the subject will be maintained
- **For research involving more than minimal risk**, an explanation as to whether any compensation, and an explanation as to whether any medical treatments are available, if injury occurs and, if so, what they consist of, or where further information may be obtained
- An explanation of **whom to contact** for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject
- A statement that **participation is voluntary**, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits, to which the subject is otherwise entitled

Informed consent—when appropriate

- A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant), which are currently **unforeseeable**
- Anticipated circumstances under which the subject's **participation may be terminated** by the investigator without regard to the subject's consent
- Any **additional costs** to the subject that may result from participation in the research
- The consequences of a subject's decision to **withdraw from the research** and procedures for orderly termination of participation by the subject
- A statement that significant **new findings** developed during the course of the research, which may relate to the subject's willingness to continue participation, will be provided to the subject
- The approximate **number of subjects** involved in the study

Informed Consent-new elements with rCR

(9) One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

- (i) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or
- (ii) A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

Informed Consent-new elements

When appropriate

- A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;
- A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and
- For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

Voluntariness

Consent is only valid if voluntarily given, which requires conditions free of coercion and undue influence.

- *Coercion*
  - An overt threat of harm intentionally presented by one person to another in order to obtain compliance
- *Undue Influence*
  - Occurs when there is an offer of excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance.
  - Inducements that would ordinarily be acceptable may become undue influences if the subject is especially vulnerable
- Both result in persons making choices that are not congruent with their goals, values and interests

Consent Process should be described in the Protocol

Plans for the consent process (how, where, when etc.) need to be anticipated and included in the protocol:

- Where and when will consent be obtained?
- How will coercion or undue influence will be minimized?
- Will consent be done in person, or by telephone/videoconference?
- Will the consent be provided in advance of the discussion?
- Will the consent be provided electronically or in hard copy?
- How much time will the potential subject be provided to consider their participation?
- Who will answer questions from the subject?
- Will the potential subject be provided the opportunity to consult with others (family, friends, private physician) prior to providing consent?

Reviewing informed consent

Review the process and the document

- Does the *process* allow for
  - 1) transfer of information
  - 2) comprehension of the information
  - 3) a voluntary decision to participate or decline
- Does the *document*
  - 1) contain the necessary information
  - 2) present the information in a comprehensible manner

Consent untouchables

NIH Required language

- Injury language
- Privacy
- Certificate of Confidentiality

Informed Consent

Use of template assures that all regulatory elements of consent are present

IRB review process includes screening of each study by staff prior to scheduling for a meeting.

Staff review will include review of the consent form for consistency, accuracy, and readability.

Protecting privacy and confidentiality

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

- Privacy is about the person
- Confidentiality is about the data

Beneficence and IRB review of research

“Beneficence thus requires that we protect against risk of harm to subjects and also that we be concerned about the loss of substantial benefits that might be gained from research”.

  - Belmont Report

Harm/benefit assessment

Ideally, a systematic, non-arbitrary analysis.

“The IRB’s task is not to determine whether the potential participant would judge the risk worth it, instead the IRB is to determine whether the invitation is justified”.

- Oxford Textbook of Clinical Research Ethics

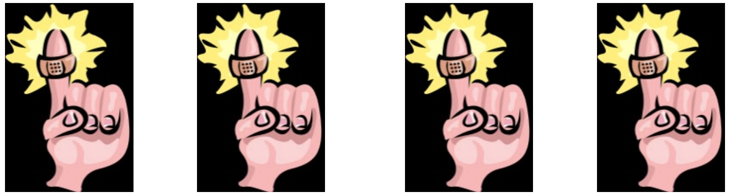
Harms and benefits

Benefits/harms to participants

- May be to individuals and/or groups
- Direct (from the research intervention)
  - From receipt of the experimental intervention
    - Uncertain
- Inclusional (clinical benefit)
  - Result from inclusion in the study, but not dependent on receiving the experimental intervention.
    - May be certain

Evaluation of harms and benefits

Low magnitude/low likelihood



Low magnitude/high likelihood

High magnitude/low likelihood

High magnitude/high likelihood

Physical Risks

Usually easiest to identify

- Drug toxicities
- Exposure to ionizing radiation
- Injuries sustained during a research related procedure
- May receive a treatment that is less effective than alternative

Considerations

- May be unpredictable and as of yet unknown
- May be delayed
- May be irreversible

Risks

Psychological

- Any psychological distress occurring as a result of participation in research.

Social

- Exist when there is the possibility that information obtained during the course of research participation could negatively impact others’ perception of the participant.

Legal

- Places participant at risk of civil/criminal liability

Economic

- Participation could have negative financial consequence

Benefits

Individual

- Access to a potentially efficacious or novel therapy
- Detection of a treatable condition

Societal

- Knowledge that will improve care of others in the future

No requirement to maximize benefit

Clinical benefits vs. Research benefits

Important in decisions about minimizing and justifying risks and assessing risk/benefit

- Consideration of existing alternatives
- Comparison to a baseline (potential benefits and risks beyond those in clinical care)

Important in participant understanding of research

- e.g. reducing possible therapeutic misconception, other misunderstandings.

Justification

Difficult to justify exposing humans to risk or inconvenience or expending resources if the knowledge expected to result has no value or is not important

(Emanuel et al. 2000; Casarett et al.2002; CIOMS 2016; Shah & Rid 2017; Wendler & Rid 2017, others)

Which benefits count when determining the reasonableness of risks?

Criteria for approval

(1) Risks to subjects are minimized:

- (i) By using procedures which are consistent with sound research design, and which 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.

Criteria for approval

- (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 (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

Applying the criteria for approval

Criteria 1: Minimize risk without interfering with scientific aims

Criteria 2: Once minimized, are risks reasonable in relation to anticipated benefit to subjects (if any), or the importance of the knowledge to be gained.

Data safety monitoring

- (6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
  - Data and safety monitoring plans need to be calibrated to the study.
    - Range from a formal DSMB/DMC with external membership to monitoring by the PI

Justice

Principle

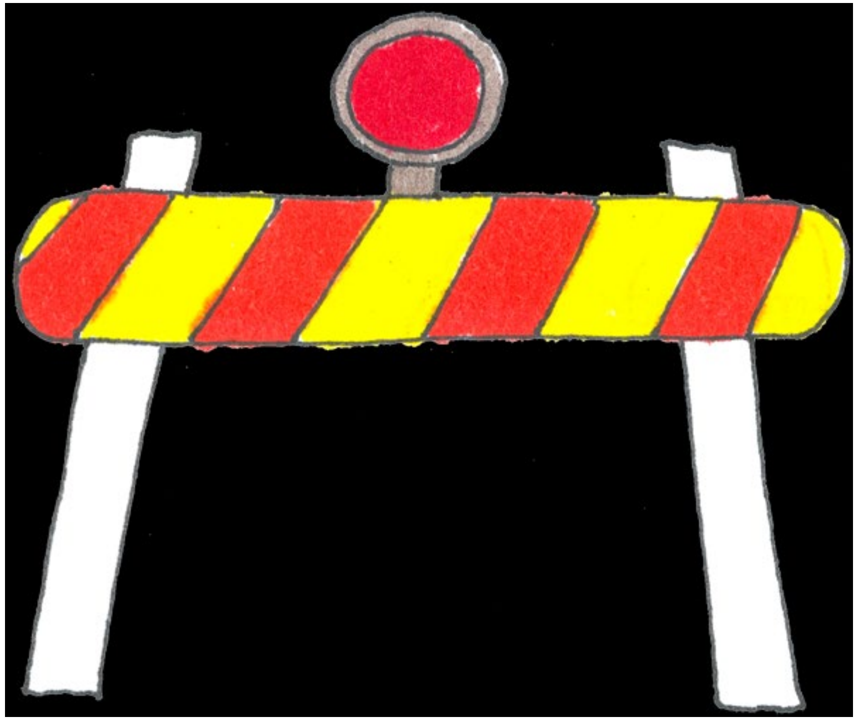
- “Equals ought to be treated equally and unequals unequally.”-Aristotle
- Distributive justice
  - Distribution of a scarce benefit
  - Distribution of burdens

Norms

- People must be treated fairly
  - Not the same as treating everyone equally
- People should be neither unfairly targeted nor unfairly excluded

2 views of Justice

PROTECTIONIST



ACCESS

Justice is about fairness

- Individuals and groups should neither be unfairly targeted nor unfairly excluded.

The Bottom Line

Justice: Criteria for approval

- (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 and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

What determines appropriate subject selection?

The most important determinant of subject selection is the scientific question.

- The population enrolled should be the one that is best able to answer the scientific question.
- Determined by the Inclusion/Exclusion criteria.

How to evaluate equitable subject selection

Are the I/E criteria appropriate for the study?

How are participants being recruited?

- Does it suggest targeting a population of convenience?
- Does it miss an important population that might benefit?

Is the inclusion of vulnerable subjects justified?

At continuing review, there is no requirement that there is proportional representation of race/sex etc. in a study.

Special protections

Diminished autonomy

- Children
- Cognitively impaired

Pregnant women?

- Fetus is the vulnerable entity

Prisoners

Economically/socially/educationally disadvantaged

Desperately ill/dying?

Research with Children

Research involving minors as participants must meet the criteria spelled out in Subpart D in addition to the Criteria for Approval (45 CFR 46.111, 21 CFR 56.111)

Children—Risk vs. Benefit

Adults:

- Risks balanced against either direct benefit or importance of anticipated knowledge

Children:

- Investigations that pose more than low risk CANNOT be justified by the importance of the anticipated knowledge.
- If risk is more than low, there MUST BE a prospect of direct benefit. The benefit must be comparable to available alternatives.

46.404/50.51-minimal risk

§46.404 Research not involving greater than minimal risk.

- HHS will conduct or fund research in which the IRB finds that no greater than minimal risk to children is presented, only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in §46.408.

Minimal risk (absolute standard)

- The risk of everyday life (normal healthy kids living in a safe environment with prudent parents)

46.405/50.52

§46.405 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.

HHS will conduct or fund research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, only if the IRB finds that:

- (a) The risk is justified by the anticipated benefit to the subjects;
- (b) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
- (c) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in §46.408.

What is direct benefit?

A benefit is direct if:

- It accrues to the individual research participant
- Is a result from the specific research intervention or procedure, and not from ancillary benefits.
- *“Prospect of direct benefit should result from the research intervention or procedure being studied (e.g., the investigational drug or medical device) and not from ancillary interventions or procedures, such as physical exams done as part of the trial” (FDA)*

What is not direct benefit?

Most diagnostic and monitoring procedures (blood draw, CT scan, biopsies etc.) unless

- that information is critical for assessing the safety of another intervention that does offer PDB, or
- would result in detection of a treatable condition that would not otherwise have been detected

More frequent visits to the doctor

Getting medications for free

46.406/50.53

§46.406 Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.

HHS will conduct or fund research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject, only if the IRB finds that:

- (a) The risk represents a minor increase over minimal risk;
- (b) The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
- (c) The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
- (d) Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth in §46.408.

What is a minor increase over minimal risk?

A slight increase over minimal risk that poses no significant threat to the child's overall health or well-being.

Any potential harms with the intervention or procedure should be expected to be transient and reversible and the probability for severe pain, discomfort, or harm should be extremely small or nonexistent.

Consider the setting and the experience level of the investigator when making an assessment as to whether an intervention or procedure meets criteria

Not otherwise approvable

If the IRB is unable to determine that the research meets the requirements of previous categories

- IRB determines that the research presents an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of children.
- Referred to a national panel to determine that it either meets other criteria or that research is justified by the importance of the knowledge sought and would not contravene the principles of respect for persons, beneficence and justice

§46.407 Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

Assent

Assent is always required, unless waived by the IRB

Requirement for assent may be waived if:

- Capability is so limited that the child cannot be consulted or
- Prospect of direct benefit important to the child's health available only within the research context
- Minimal risk research that could not otherwise be conducted.

Assent is an affirmative statement

- Failure to object cannot be taken as assent.

General guidelines

- Assent waived (very young)
- Oral Assent (young)
- Written Assent
  - Age-appropriate document
  - Actual consent (13 and up?)

Cognitively impaired—NIH policy 403

Category A: The research is minimal risk

Category B: The research is greater than minimal risk, and offers a prospect of direct benefit to the participant

Category C: The research is no more than a minor increase over minimal risk with no prospect of direct benefit, and does not adversely affect the rights, safety, or welfare of the participants

Category D: Research does not meet the above conditions but has undergone additional institutional review and approval by the NIH IO

Cognitively impaired

The protocol should explicitly justify the rationale for enrollment of those who lack consent capacity and, as applicable, what safeguards will be in place.

Consider whether inclusion of individuals who lack consent capacity is ethically appropriate and scientifically necessary (e.g., the research aims to improve understanding, detection, diagnosis, or treatment of the disorders that cause the incapacity).

Can the scientific question be answered by studying individuals who retain consent capacity?

Consider if the method to assess capacity as described in the protocol, as well as plans for who will provide this assessment, are adequate.

Investigator should propose what level of assent should be sought from this population

Pregnant women—being included

There are specific regulations around the inclusion of pregnant women in research: *45 CFR 46.204: Research involving pregnant women or fetuses*

- One of the conditions: *The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit,* ***the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means****.*
- If the study does not intentionally enroll or exclude pregnant subjects, but it is possible for a participant to become pregnant while on study, and the researcher intends to keep the participant on the study during the pregnancy, then the protocol must provide sufficient justification for their continued inclusion in the research.
- If the study is minimal risk, the researcher may not specifically address the issue in the protocol inclusion if not scientifically relevant. However, if the protocol contains research procedures that in the context of standard medical care require a negative pregnancy test, the protocol will need to include this test/state it must be negative.

Pregnant women—being excluded

In studies that explicitly exclude pregnant subjects, if a participant becomes pregnant while on study and the researcher wishes the to keep the participant on study, then a MOD must be submitted to provide the justification for continued participation of the pregnant subject on the research.

Because the potential benefits of research participation may extend to pregnant subjects, the rationale for excluding pregnant subjects from a specific protocol should be explicitly stated.

Key Points

The regulatory criteria for approval flow directly from the core ethical principles.

The criteria are both necessary and sufficient to assure the protection of human subjects and that the studies we approve are ethical.

Every reviewer, whether physician, scientist, non-scientist, affiliated or non-affiliated, can (and must) apply all the criteria.

Resources

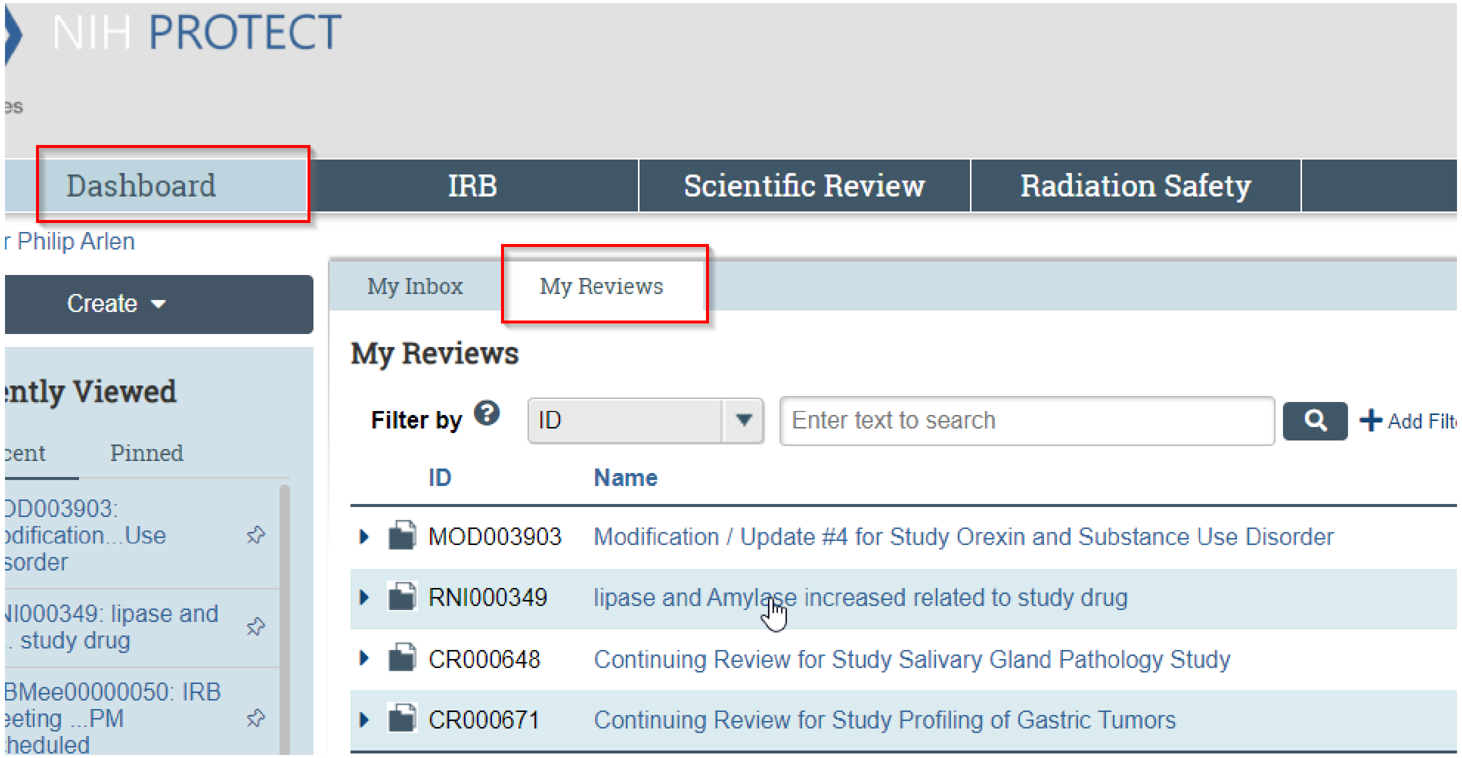
The Belmont Report

- http://ohsr.od.nih.gov/guidelines/belmont.html

Levine, Robert J. Ethics and Regulation of Clinical Research, 2nd ed. Urban & Schwarzenberg 1986

The Oxford Textbook of Clinical Research Ethics. Emanuel, E.J. et al Editors. Oxford University Press. 2008
Acknowledgements: Jeff Cooper, The Huron Group.

How to review a protocol: The nuts and bolts



My Reviews

ID	Name
MOD003903	Modification / Update #4 for Study Orexin and Substance Use Disorder
RNI000349	lipase and Amylase increased related to study drug
CR000648	Continuing Review for Study Salivary Gland Pathology Study
CR000671	Continuing Review for Study Profiling of Gastric Tumors

COI

You should self identify if you have a conflict of interest on a study

- Financial
- Engaged team member
- Other

May answer questions about study, but not be present for discussion or vote

Role of Scientific reviewer

IRB review is not NIH peer review or merit review.

- Scientific reviewers should be able to explain protocol to non-scientific members
- Scientific review should address these questions:
  1) Is there a safer way to perform the research that would still accomplish the research aims?
  2) Are there procedures that would reduce subject risks without negatively affecting the research?
  3) Does the protocol accurately describe the risks?
  4) Does the protocol accurately describe the benefits?
  5) Is the protocol likely to yield the knowledge proposed to result
- Scientific review is not about redesigning the protocol

The non-scientist IRB member

What is the role of the NS?

- Present a viewpoint that comes from outside the scientific world
- Be able to review without the intrinsic conflicts that scientific/affiliated reviewers have.
- Look at things from the participant perspective.

Don’t try to review as a scientific reviewer.

Don’t let jargon intimidate.

Don’t focus only on consent.

You are still voting on all criteria.

Full Board Review

Primary reviewer process

- Studies assigned to a primary and secondary reviewer
- All committee members should have some familiarity with each action prior to meeting

Resolve issues prior to meeting

- Contact PI either directly using the clarification activity in PROTECT, or can use IRBO staff as intermediary if you wish to maintain anonymity

Vote at end of discussion

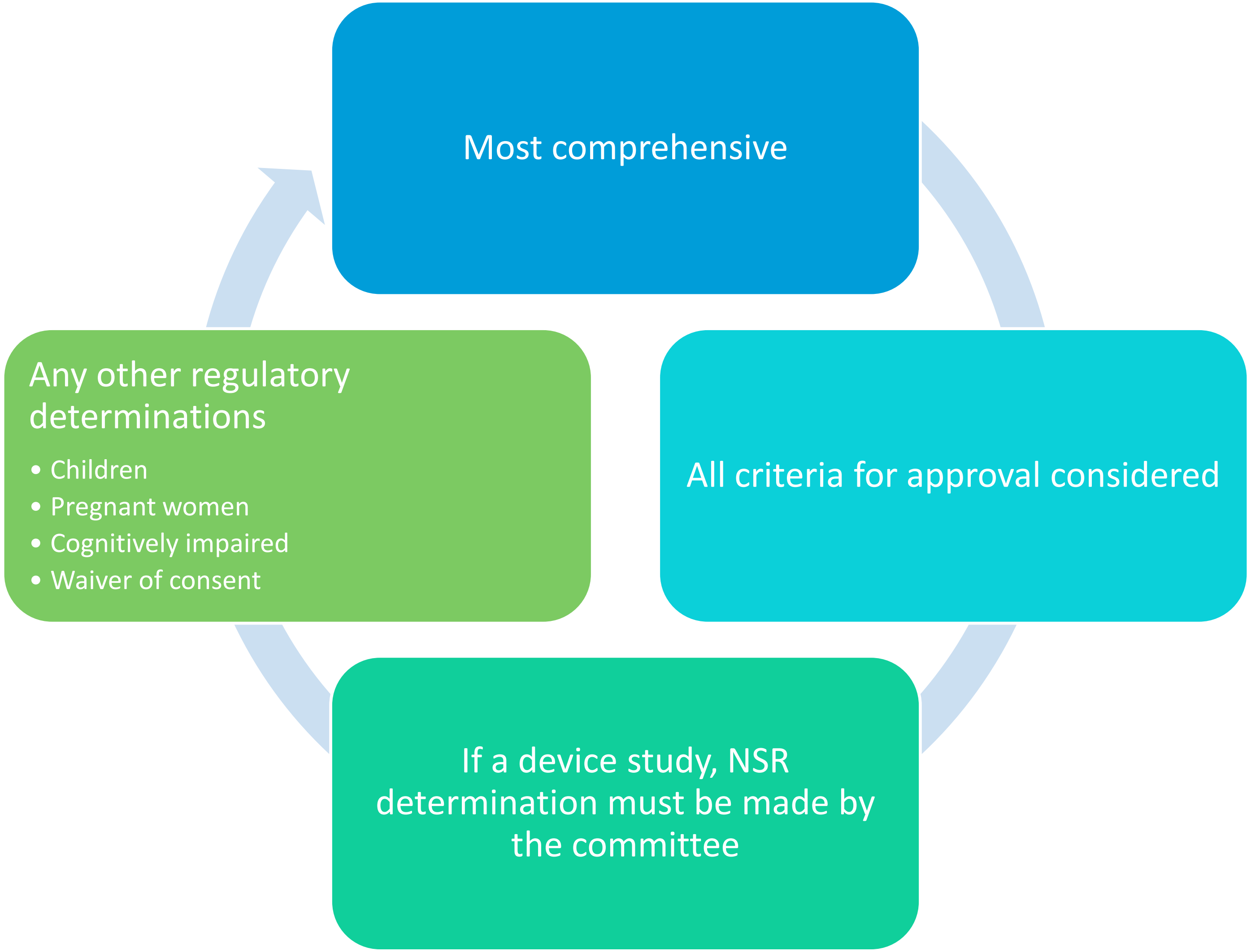
- Approve
- Approve with stipulations (modifications required to secure approval)
- Deferred (must come back to committee)
- Disapprove

Specific Regulatory determinations as needed

Types of reviews

- New Protocols
- Continuing reviews
- Modifications (mods)
- Potential unanticipated problems (reportable new information)

New protocol reviews



Most comprehensive

All criteria for approval considered

If a device study, NSR determination must be made by the committee

Any other regulatory determinations

- Children
- Pregnant women
- Cognitively impaired
- Waiver of consent

What documents should I look at?

The IRB application

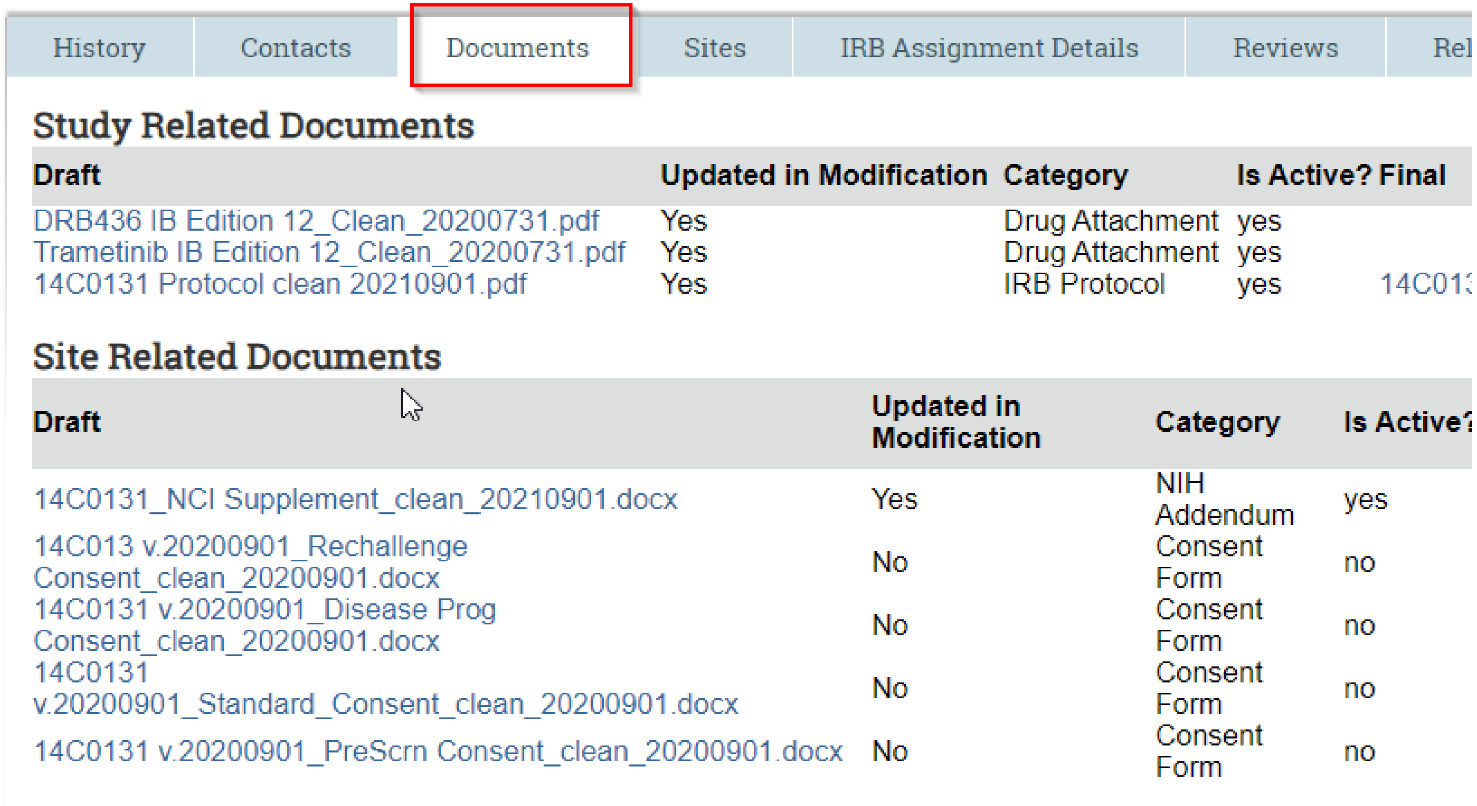
The study protocol

The IB or package insert

The consent document

Data collection instruments

Recruitment materials



Study Related Documents

Draft	Updated in Modification	Category	Is Active?	Final
DRB436 IB Edition 12_Clean_20200731.pdf	Yes	Drug Attachment	yes	
Trametinib IB Edition 12_Clean_20200731.pdf	Yes	Drug Attachment	yes	
14C0131 Protocol clean 20210901.pdf	Yes	IRB Protocol	yes	14C013

Site Related Documents

Draft	Updated in Modification	Category	Is Active?
14C0131_NCI Supplement_clean_20210901.docx	Yes	NIH Addendum	yes
14C013 v.20200901_Rechallenge Consent_clean_20200901.docx	No	Consent Form	no
14C0131 v.20200901_Disease Prog Consent_clean_20200901.docx	No	Consent Form	no
14C0131 v.20200901_Standard_Consent_clean_20200901.docx	No	Consent Form	no
14C0131 v.20200901_PreScrn Consent_clean_20200901.docx	No	Consent Form	no

Investigational device determinations

Investigation	• A clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device (21 CFR 812.3(h))
Investigational device	• A device, including a transitional device, that is the object of an investigation. (21 CFR 812.3(g))
Investigational device exemption	• Refers to the regulations under 21 CFR 812 • An approved IDE means the IRB (and FDA for significant risk devices) has approved the sponsor’s study application, and all the requirements under 21 CFR 812 are met

Investigational devices

Significant Risk (SR) investigational device

- intended as an implant & presents potential for serious risk to the health, safety, or welfare of a subject
- purported/represented to be for use in supporting/sustaining human life & presents potential for serious risk to health, safety, or welfare of a subject
- use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to health, safety, or welfare of a subject **or**
- Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject
  - *IDE approval from FDA and IRB approval required*

NSR Device

- Does not meet the definition of a SR device study
  - *Only IRB approval required*

Continuing reviews

Start from the presumption that the previous review was adequate and appropriate.

Focus is on progress of the study

Any changes/new information that affect the approvability of the study?

Anything that might alter willingness of subjects to continue/enroll?

- New risk information?
- New data in the literature?

Continuing reviews (continued)

Assess enrollment progress

- Will they ever meet their goal?

Have there been problems?

Lots of withdrawals?

DO NOT NEEDLESSLY TINKER WITH THE CONSENT!

What if I find problems?

- Are they important for the approvability of the study?

Modifications

Changes to a previously approved protocol that are more than minor

Have the potential to adversely affect the risk/benefit analysis

Significant change in aims or study design.

Your review should focus on whether the proposed change alters the “approvability” of the study.

Outcome options

- Approve
- Approve with stipulations (modifications required to secure approval)
- Deferred (must come back to committee)
- Disapprove

For MODs: Specific regulatory determinations as needed, e.g.:

- Pediatric category
- Number of signatures required
- Assent

Stipulations

- Must relate to a regulatory criteria for approval
- Must be prescriptive
- Any required changes to study documents (except typos, grammar etc.) must be discussed and voted on during meeting
- “Suggested” changes/recommendations are not appropriate – focus on changes required for approval.

Reviewer presentations

- Present key elements of study
  - Be concise!
    - “This is an industry sponsored, multi-center phase 2 trial comparing std care vs std care plus investigational drug x in the treatment of disease y.
    - Don’t go into a long, detailed description.
- Think about criteria for approval in organizing your presentation.
  - Review checklists are available for you to use in PROTECT
    - Does the study meet the regulatory criteria for approval?
    - If not, which criteria?
  - If device study, is it SR/NSR?
  - Children? Other special populations?

Reviewer presentations

Don’t expect or attempt to resolve major issues about the study at the meeting.

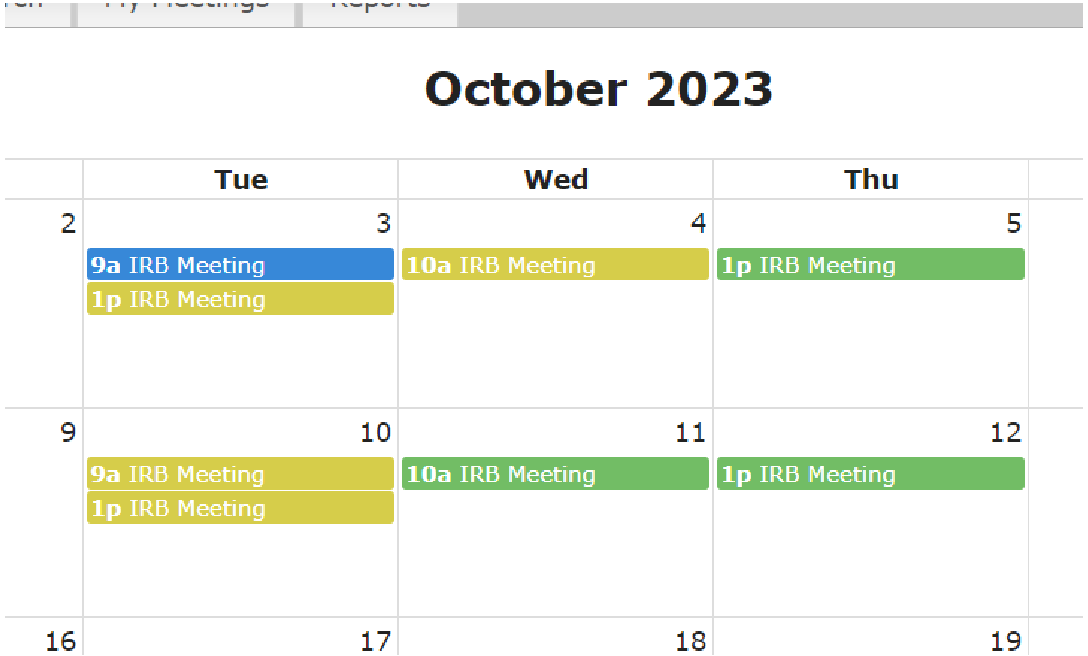
- Do that beforehand!

If not much needs to be said, don’t say much.

Don’t be offended if chair moves the discussion along.

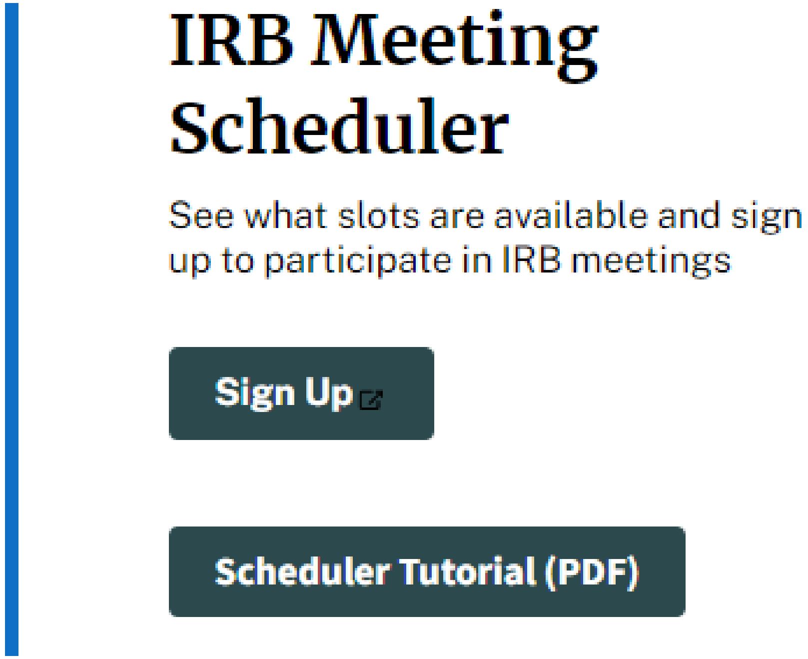
Don’t excessively wordsmith the consent or read it like a legal contract.

How to sign up for a meeting



October 2023

	Tue	Wed	Thu	
2	3 9a IRB Meeting 1p IRB Meeting	4 10a IRB Meeting	5 1p IRB Meeting	
9	10 9a IRB Meeting 1p IRB Meeting	11 10a IRB Meeting	12 1p IRB Meeting	
16	17	18	19	



IRB Meeting Scheduler

See what slots are available and sign up to participate in IRB meetings