TIPS & TRICKS FOR AVOIDING STIPS:
HOW TO INCREASE THE ODDS OF ACHIEVING SPEEDY IRB APPROVAL

Julie M. Eiserman, MA, CCRP
Team Lead, OHSRP, IRBO

Protocol Navigator Work Group Meeting

May 11, 2023

AGENDA

- Background & Context
- Common Pitfalls & Tips to Avoid Them
- Sticky Issues: Frequently “Stipped” Topics
- Key Points to Remember
- Other Tips & Resources
- Questions

BACKGROUND, PART I

Under the new centralized HRPP, we have discovered that in some cases, the previous NIH IRBs had atypical interpretations of the regulations and OHRP guidance. Also certain regulations or guidance were not applied.

Found missing or inaccurate content in protocols and missing determinations in the IRB minutes, e.g. waiver of consent, nonsignificant risk device determinations, justification for involvement of pregnant women

Some former IRBs had unique requirements due to certain ethical concerns, e.g. informed consent for data sharing.

BACKGROUND, PART II

The IRB currently supports many protocols that were initially opened 20, 30, and even 40+ years ago. A significant number of these protocols are still open for enrollment.

- These protocols may have met the regulatory criteria for IRB approval when they were initially reviewed, but at our review, we have found that often they do not.

Regulations, guidance, and policies that affect human subjects research are constantly evolving to include new requirements and spawn even more policies.

- Some PIs have struggled to keep their protocols up-to-date over time.

CONTEXT

- IRBO consistently striving to ensure that all IRB-approved studies are compliant with regulations and policy
- Rely on the Research Teams and Navigators to make sure that the content of protocols and consent forms are up-to-date
- Want to support Navigators/Study Coordinators to identify issues, bring them to the attention of the PIs, and submit well-written modifications

COMMON PITFALLS & TIPS TO AVOID THEM

FAST IS FINE, BUT ACCURACY IS EVERYTHING.

--Wyatt Earp

INACCURATE CONTENT IN RECRUITMENT MATERIALS

COMMON PITFALL: A research team relies on the Office of Recruitment Services or an external contractor to create their recruitment materials. This may result in recruitment materials with missing or inaccurate content (e.g. that the study provides benefit or treatment) or misleading content (e.g. highlights payment without discussing procedures).

CONFIRM ACCURACY & COMPLETENESS OF RECRUITMENT MATERIALS

TIP: Prior to submitting any recruitment materials, carefully review them to confirm that the content is relevant to the specific study and that the key inclusion criteria and study procedures are addressed.

INADEQUATE CHANGES & INCONSISTENCIES

COMMON PITFALL: The IRB receives a MOD with one change to the protocol that should trigger additional changes to the protocol/consent, but they were not made.

For example, a new research procedure might be added to the protocol, but the procedure is not described with sufficient detail, no risk language is included, or no information is provided about the tool or device that will be used to conduct the procedure.

There may be inconsistencies across documents, e.g. the protocol discusses a research procedure, but the consent form is not revised to describe the procedure; compensation is revised in the protocol but not in the consent forms.

CONCISE LANGUAGE, PROVIDE DETAIL & DOUBLE-CHECK

TIPS: When making a significant change, be sure to use clear, concise language and ensure that there is adequate detail.

Review the protocol, consent form and all study subject-facing documents that might be affected by the change and revise them accordingly.

MISUSE OF TEMPLATE LANGUAGE

COMMON PITFALL: The IRB receives a MOD which involves adding NIH Protocol template or Consent Library template language. However, the template language has not been revised to be specific to the study and the existing protocol content has not been revised in consideration of the new language.

As a result, the document may now include contradictory or duplicative language or information that doesn't apply to the research study. Finally, the location of the added language may result in the reader having trouble following the content.

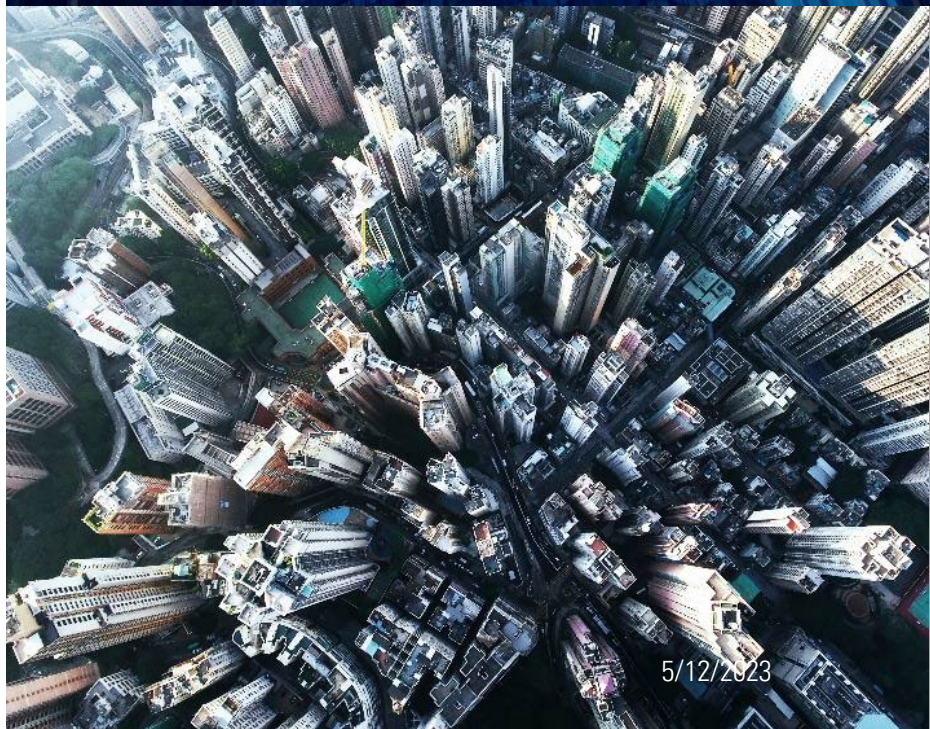
REVIEW & REVISE WHEN USING TEMPLATE LANGUAGE

TIP: When incorporating any template language, carefully review the language to ensure that what is being added applies to the specific study. Then revise the entire section including the added language to remove any redundancies and contradictions; and ensure that it is accurate and easy-to-follow.

STICKY ISSUES: FREQUENTLY "STIPPED" TOPICS

FREQUENTLY "STIPPED" TOPICS

- There are some topics that tend to trigger more stipulations than others because:
  - There have been changes in the HRPP policies (from the previous SOPs) or other NIH policies; or
  - OHSRP leadership has a new stance on how a part of the regulations is to be implemented in the NIH IRP.
  - They are complicated and difficult to understand.
- **These topics require extra attention to get them "right".**



TOPICS REQUIRING EXTRA ATTENTION

- INCLUSION OF PREGNANT PEOPLE
- ENROLLMENT OF NIH STAFF
- COLLECTING IDENTIFIABLE DATA ABOUT FAMILY MEMBERS/PREGNANT PARTNERS

- INVESTIGATIONAL DEVICES
  - Description in the protocol and consent
  - MRI Devices
  - Device section in PROTECT
- GENETIC RESEARCH/ WGS/WES
  - Description in the protocol
  - Consent for genetic testing/WGS/WES
  - Return of results
  - Consent For sharing genomic Data

- CONSENTING
  - Remote Consent vs. Electronic Consent
  - Electronic Consent vs. Electronic Signature
  - iMedConsent
  - Notification/Re-Consent

KEY POINTS TO REMEMBER

INCLUSION OF PREGNANT PEOPLE

- Greater than minimal risk studies should explicitly state whether pregnant people may enroll or not.
    - If pregnant people will be excluded, must discuss rationale, specific pregnancy testing and contraception requirements, planned actions in event of pregnancy, and potential risks of future fertility. See the Consent Library for guidance on consent.
- If the protocol states that pregnant people will be included, it must address the requirements under 45 CR 46, Subpart B.
    - **Must include a justification**, e.g. an objective of the study could not be met without enrolling pregnant people
    - Refer to HRPP Policy 400 for further guidance

KEEPING SUBJECTS WHO BECOME PREGNANT ON STUDY

If the study does not intentionally enroll pregnant women, but the PI intends to keep an enrolled participant who becomes pregnant on the study (pregnancy is not an off-study criterion), then the protocol **must also include a justification**.

ENROLLMENT OF NIH STAFF

When research offers **no prospect of direct benefit** to NIH staff (or immediate family of a study team) who enroll, the protocol must comply with HRPP Policy 404, i.e.:

- Include planned safeguards for recruitment, consenting, collecting private information
- State NIH staff will be referred to the NIH Frequently Asked Questions (FAQs) for NIH Staff Who are Considering Participation in NIH Research
    - "The NIH information Sheet" is no longer in existence.

COLLECTING IDENTIFIABLE DATA ABOUT FAMILY MEMBERS

- Collecting data about family members (e.g. extensive family health history, partners who become pregnant during the study, parents of minor subjects), along with identifiers, transforms these individuals into research subjects.
  - Protocol must then:
    - Contain a discussion of them as part of the study population
    - Include an appropriate plan to recruit and consent them to the study or make the case for a waiver of consent

- Partners (of the subjects), who become pregnant during treatment studies, can be enrolled in Dr. Guptill's NIH Pregnancy Registry protocol in order to follow the pregnancy and track outcomes

INVESTIGATIONAL DEVICES

- When devices are used as part of a study:
  - The PI must first determine whether the device meets the definition of a medical device.
  - If a medical device is being used to answer the research question (i.e. not as part of standard clinical care), the protocol must:
    1. Include name of the device and the manufacturer;
    2. Describe how the device is being used and its purpose;
    3. State whether the device is FDA-cleared and if so, whether they are being used per labeling or not; and
    4. When the device is not FDA-cleared (or is being used "off-label"): Make the case that the device meets the criteria to be IDE-Exempt, a Nonsignificant Risk device or a Significant Risk device.
  - Refer to the protocol templates for more information.
  - The devices used as part of the research that are not that are not FDA-approved should be disclosed in the consent form.

MRI DEVICES

- All MRI-related devices that are **not FDA-cleared (or being used off-label)** should be considered investigational, whether or not the PI views them as being the object of the research.
    - Examples of MRI devices that might not be FDA-cleared: MRI scanners, *research* pulse sequences, *research* coils, *research* imaging reconstruction and analysis software
- Refer to the Guideline for Device Classification for Protocols using MRI in the NMR Center for more information about MRI devices and refer to the Consent Library for template language about unapproved MRI devices.

DEVICES SECTION IN PROTECT

All medical devices or devices that are not FDA-cleared or being used off-label (and are being used to answer the research questions) must be listed in the device section as an investigational device.

DEVICES SECTION IN PROTECT

1. * **Select each investigational device or HUD being used as part of the study:**

Device	Device Manufacturer	Attachment Name
Deep Brain Stimulator	Medtronic Corporation	
Subdural Surface Electrodes	PMT Corporation	

2. * **Device exemptions applicable to this study:** AbbreviatedIDE

3. **Attach files:** (such as IDE, HDE, or other information that was not attached for a specific device)

Document	Category	Date Modified	Document History
There are no items to display			

1. Add each device by searching. If you can't find the device name, first look at the device report on the IRB Report Tab. If it isn't listed, request that it be added by putting in a ticket here.
   - If there is no external manufacturer, the manufacturer is NIH.
   - No need to add a manufacturer for research pulse sequences.
   - Attachment: Upload documentation from the external manufacturer about the device (e.g. device description, device manual, etc.)
2. If all devices meet the criteria of a nonsignificant risk device, choose "Abbreviated IDE".
3. If the study team received an opinion about the device or an SR IDE from the FDA, upload the documentation in this section.

GENETIC RESEARCH/WGS/WES

- Any protocol that proposes genetic research/WGS/WES must address:
  - The purpose, what specimens will be utilized, and what type of genetic data will be generated
  - Privacy and confidentiality considerations
  - Plan for return of primary results (or no plan)
  - Plan for return of secondary genomic findings or incidental findings, when applicable
  - Genetic Counseling (if results will be returned)

- Refer to the protocol templates for more information.

CONSENT FOR GENETIC TESTING/ WGS/WES

- If genomic sequencing (WGS or WES) is being done on samples collected on or after August 31, 2015, there should be prospective informed consent* from the subjects.
  - *Contact OHSRP for requests for exceptions.*
- If the investigator wishes to return results to subjects, there must be prospective consent* for the genetic testing/genomic sequencing, prior to returning any results to subjects.
  - You should not contact a participant with a genetic result, unless they have consented to genetic testing/genomic sequencing.
- Refer to the Consent Library for explicit guidance and template language.

RETURN OF RESULTS

- Genetic results can only be shared if they were generated in a CLIA-certified lab (i.e. results from a research lab cannot be shared).
- If it's necessary to obtain a second sample for confirmatory testing in a CLIA-certified lab, the subject cannot be told about the possible finding, prior to the testing.
- As of Oct. 1, 2022, new studies that involve genomic sequencing must include a plan in the protocol and consent for returning clinically actionable secondary genomic findings (or provide a justification for not doing so).
- Refer to the IRB Guidance for Return of Secondary Genomic Results in the NIH Intramural Program, the protocol templates, and the Consent Library for more information.

CONSENT FOR SHARING GENOMIC DATA

- If the investigator plans to comply with the GDS Policy, and the specimens were collected on or after August 31, 2015, the consent form must include:
  - A statement about genomic and phenotypic data being shared broadly for future research purposes; and
  - An explanation about whether participants' individual-level data will be shared through unrestricted- or controlled-access repositories
  - Refer to the OHSRP Sharing Data and Specimens webpage and the NIH Genomic Data Sharing Policy webpage for more information about the GDS Policy

REMOTE CONSENT VS ELECTRONIC CONSENT

- When addressing remote consent and electronic consent in the protocol, make sure that the language reflects the research team's actual consenting plan.
- The terms remote consent and electronic consent are not synonymous.
  - Both processes require prospective IRB approval
- Remote consent means that the consenting investigator and the subject are NOT co-located; typically the subject is off-site.
- Remote consent could be conducted via telephone or an NIH-approved audio-conferencing or video-conferencing platform.
  - Andor is now the only approved technology that can be used for consenting or conducting telehealth with NIH CC patients who are in the US.
- Refer to Obtaining Consent Using a Remote or Other Alternative Process

REMOTE CONSENT VS ELECTRONIC CONSENT, CONT.

- An approved remote consent process could involve a paper consent form with a wet signature; an electronic consent form with a signature being created via a finger, stylus or mouse (e.g. iMedConsent); a paper or electronic consent form with a waiver of documentation (no signature); or a verbal script.
- Electronic consent generally refers to viewing an electronic consent document on a computer, cell phone or tablet.
  - Unless there is a waiver of documentation, "documentation of consent" (i.e. the signature) is made on the electronic document.
- Refer to Obtaining Consent Using a Remote or Other Alternative Process

ELECTRONIC CONSENT VS ELECTRONIC SIGNATURE

- When electronic consent or an electronic signature in a protocol, make sure that the language reflects the research team's actual plan.
- An electronic signature means that the signature is digitally generated by a program rather than a "hand", i.e. the program stamps the consent form with the signature and the date and time.
- NIH investigators can be approved to obtain an electronic signature as long as the investigator includes a plan to verify the identity of the subject.
- If the study is FDA-regulated, the program being used to collect the digital signatures must be verified as being 21 CFR, Part 11 compliant.
- Refer to Obtaining Consent Using a Remote or Other Alternative Process

IMEDCONSENT: DID YOU KNOW?

- iMedConsent is an application offered through the NIH CC Health Information Management Division that allows the collection of signatures and the checking of boxes on an electronic consent document.
- iMedConsent is 21 CFR, Part 11 compliant.
- The signature is captured via finger, stylus or mouse, i.e. **an electronic consent process without an electronic signature.**
- iMedConsent can be used either off-site or on-site at the NIH CC.
- Any study that uses CRIS for its subjects can use iMedConsent for consenting.
- Within the next few years the plan is for all consent signatures to be captured via iMedConsent, regardless of the consent process or the location of the subject.

PLAN FOR NOTIFICATION/ RE-CONSENT

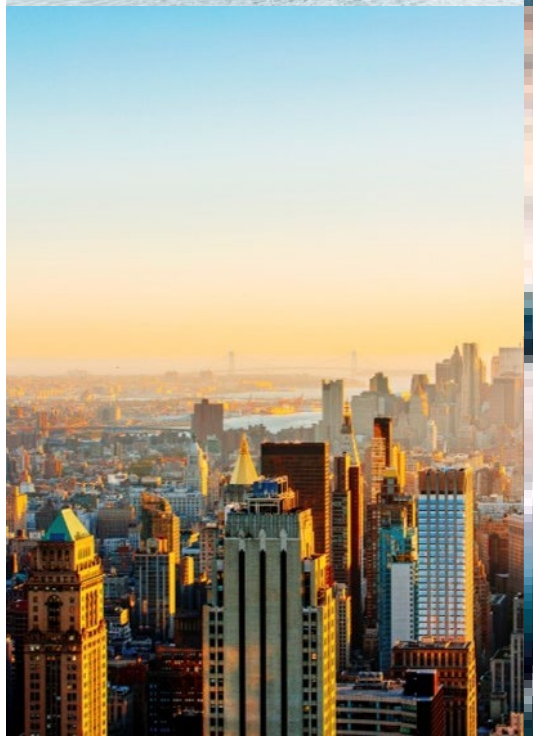
- When submitting a MOD about a change in the PI, study contact, procedures, or risks, or to address new findings:
  - Either include a plan and process for notifying or re-consenting active subjects, or a justification for why you don't plan notify subjects
    - Be clear about who will be notified; when they will be notified; and how they will be notified
    - Revise the consent form and/or attach a phone script or information letter
    - Refer to the presentation, Re-consent and Subject Notification: Expectations and Flexibilities for Complying with the Common Rule for more information.

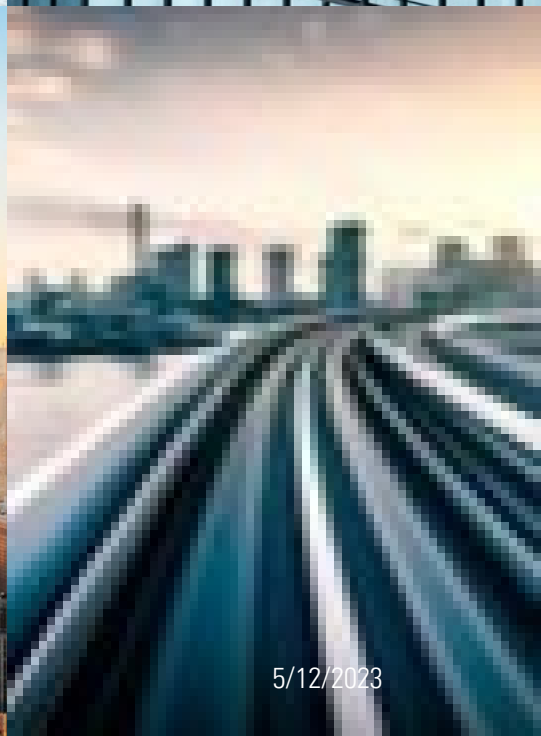
OTHER TIPS & RESOURCES

- Save copies of stipulations + revised protocols and consent forms which address these issues to reference for future IRs or Mods
- Continue to refer to and review the NIH protocol/consent templates, HRPP policies and guidance, the Consent Library, etc.
- Review the presentations (with recordings and slide decks) in the Presentation Archive which address these topics
- Check the Researchers' page, Alternate Consent Processes or FAQs for relevant content
- When in doubt, reach out to your IRB Team members or email IRB@od.nih.gov.

IN SUM

If there are steps that we can take or information that we can provide to help support your work, please feel free to reach out.





THANK YOU

For more information, feel free to email us @ irb@od.nih.gov or check out the OHSRP Website: https://irbo.nih.gov/confluence