Reviewers Guide on Clinical Trials

Office of Research Integrity & Compliance | Version 2
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This document is meant to help board members conduct reviews for Full Board: Clinical Trial submissions. CITI ethics training will be checked by the ORIC staff; no protocol will be approved until the training requirements are met. The typical questions that are in the other submission type's Questionnaires are not present for the Full Board: Clinical Trial submission because the information should be included in the external sponsored protocol document.

If further assistance or clarification is required, please contact the ORIC at 304-293-7073, or at IRB@mail.wvu.edu.

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Personnel

The PI must address these two points in their qualifications summary:

1. The PI's role/affiliation with WVU (i.e. professor of Biology, or clinician at Ruby Memorial, etc.)
2. Research experience (i.e. 10 years of experience conducting research)

A student or resident may never be the PI on a study. If the PI is not the person qualified to perform all the procedures in the protocol (i.e. PI is an engineer but surgery is required), the reviewer/board may require that a person with the correct qualifications be added to the research team.

Note: The delegated task of each research team member can be found on this page.

Notes & Attachments

The intent of the 'Notes' section is for PI's to respond to revisions requests. Sometimes, investigators respond by attaching a supporting document. If a protocol is resubmitted, it is recommended that the reviewer check for a note before proceeding with the review.

Note: All clinical trials must be accompanied by a written protocol narrative either from the sponsor or from the physician if this is a physician initiated study. Externally sponsored studies require an investigator brochure.

All file attachments can be accessed from either the Notes & Attachments tab, as well as the Protocol Summary tab.

Protocol Summary

All information, excluding 'Notes from the investigator', can be found in this section of the protocol. This section of the guidance will go through each area of the protocol submission and what appears in the summary.

Personnel

This section gives a quick overlook of the PI and research team. Specifics can be found under the *Personnel* tab.

Human Subject Research

All three answers should be yes. If not, it may not be human subject research, needs to be flagged and sent back.

Funding Source

There needs to be a yes or no response. We are interested in knowing who is paying for the study, if anyone. If the PI is receiving external funding, it needs to be mentioned in the consent form.

If the sponsor is external to WVU, there must be a sponsored protocol and an investigator brochure (for drugs and devices) attached to the submission.

Locations of Research

A location needs to be selected. If the study is conducted at an off-site facility (non-WVU), a letter of permission from that location needs to be in the *Attachments* section.

If the location of research is international, you must consider:

1. Whether the questions and consents require translation in another language, if so, there must be a letter verifying that the translation is accurate. The letter must be from an expert who is not involved in the study.
2. A letter is needed from an expert that the questions and methods will not violate any cultural norms of that culture. The letter must come from an expert who is not part of the study.

Note: The two letters may be combined in one document and signed by one person.

WVU needs to be aware if a WVU person is collaborating with another institution. For example, this can be in the form of a project both are working on, shared data, or data analysis. This should be explained in the design or summary.

- If there is a collaboration effort on the research, an Inter-Institutional Authorization Agreement (IAA) should be attached.

The final question in this section is intended to identify if there is more than one institution conducting the very same protocol, such as commercially sponsored research.

- We are not asking if the WVU PI is recruiting or conducting procedures at more than one site.

HIPAA

To be covered by HIPAA, a study must ask for medical information such as blood pressure, diagnosis, etc. and have an identifier. Please refer to the HIPAA Identifiers Guidance. Anytime medical charts are involved there is HIPAA.

Surveys can also be covered by HIPAA if they ask questions such as 'do you see a doctor for your illness?' 'Do you take medication when you have a cold? What type of medicine?' This information must also be identifiable in order to be covered under HIPAA.

If the response to HIPAA is yes then the PI must choose which HIPAA form will be used. All HIPAA forms and consent forms with HIPAA language are on the Forms Page of the ORIC website. Applicable forms must be attached in the submitted protocol.

- For any study with a consent form, HIPAA information should be part of the consent form, i.e. Only Minimal Risk with HIPAA consent. The consent form will state this in the upper right corner. This is the first option after the "is this PHI" question.
- For studies without a consent form, or if records are reviewed before approaching subject for consent then the HIPAA waiver form should be chosen and the HIPAA waiver attached. Any retrospective medical chart study must use the HIPAA waiver form.

The other options listed below should not be used in most cases. This is confusing to both reviewers and researchers, but the other options are very rare. Please send it back to request these be removed or justify why this option was chosen.

The option for authorization from the subject is ONLY for those few cases where the consent is not merged with the HIPAA. This is a separate HIPAA form to be signed by the patient.

One that may occur occasionally is: The Data Use Agreement is only for sharing HIPAA data with another institution or entity with a limited data set.

The option for HIPAA De-Identification Certification is only for non-human research subject protocols (NHSR). The decedent HIPAA form is also usually used only for NHSR protocols.

If identifiable data or samples are received or shared with another entity, a Data Use Agreement should be signed by both entities. If WVU is sharing, the PI, from the other site, should contact Legal Counsel for review before submitting.

Consent Procedures

Will signed informed consent be obtained? If this is a drug or device study the answer must be 'yes.' It can only be No if the researcher can justify a waiver.

The description of the consent process should be detailed and in chronological order (1, 2, 3): At what point in the process is consent obtained, who will do this, and where, i.e. The physician will ask the patient if they would like to be in a research study and contact the researcher. The researcher will go to the clinic and sit with the participant in a private room and discuss the consent form with the patient.

Note: Any study involving an IND or IDE must have signed consent.

If the consent needs to be translated, an expert in the language must write a letter verifying that this is a true translation of the English copy. Also an expert in the social culture of that country must write a letter that the social norms of that culture are not violated by the consent or the procedures of the study. The letters must come from person(s) not on the research team.

When answering the additional pertinent information question with a 'yes', then the subsequent response must state that a letter will be sent, a subject may be re-consented, or will be informed at the next study visit.

The Waiver of Documentation of Consent is so the requirement of a signature is not necessary during consent. A normal consent is created but the signatures are not included – as may be needed for on line consents.

Finally, anyone obtaining consent must be listed as well as how they will be trained to obtain consent. If they are not listed on the consent form, the consent should state, "This study has been explained to me by " leaving a blank where the consenter can print in their name. Anyone obtaining consent must be listed in the Personnel page.

- The exception to this rule is if there are 30 or more persons who change frequently (such as residents) – they can be listed in a separate sheet and added to the attachment section.

Advertisements

If an advertisement is used, the PI must explain what type of ad and where it will be used. It must conform to our Guidelines for Advertisements and must not be coercive in formatting or wording. The checklist for advertisements in the Online Review tab should help with this determination. Any payment amount may not stand out in the text, either by size, color or formatting.

Radiation Safety

If yes is indicated, the Radiation Safety Officer at WVU will be sent the study for sign off automatically. The IRB does not receive the study until it has received Radiation Safety approval.

Biological Safety

If IBC approval is determined to be needed, then the approval letter must be attached to the submission.

Subjects

Researchers are required to specify the maximum number of subjects to be enrolled by the WVU research team. Enrollment can occur locally, nationally, or internationally. A justification for the sample size is also required; it may be applicable to say a convenience sample or a power analysis may need to be included.

Note: It is a violation to go over that number, but enrolling less than the goal number is not an IRB violation.

Inclusion and exclusion criteria need to be clearly explained and outlined. A justification that equitable selection of subjects is needed as well (i.e. explain why only males are invited to participate).

The "identify and recruit" response should give details in chronological order (1, 2, or 3) whereas the Description of Procedures in Design should be more general. An example is:

- Medical records in a clinic are reviewed to find patients with a certain disease or condition.
- At the patient's next clinic visit the physician asks if the individual is interested in participating in a study.
- If the person says yes, the research team is contacted. The team member discusses the study with the patient in a private room. If the patient is interested, the consent form is discussed. The patient is given the opportunity to take the consent form home and discuss with their family/friends.
- At the next visit, the patient and the PI discuss any additional questions and sign the form. Upon signing, the patient is given a copy of the consent form.

If the applicant enters yes to the question regarding drugs/substances/nutrients/biologics, then a list of questions appear. If the study involves an IND there must be an IND number – in that case there must be an attachment in the *Notes and Attachments* page that verifies this. It can be in the sponsor protocol or a separate FDA letter. Off-label use of drugs needs to be discussed at the full board meeting and may require that an IND be obtained.

- If this is an IND and an external sponsor, the sponsored protocol and the investigator's brochure need to be attached.

WVU Pharmacy must be involved if the study drug is stored here. All drugs that will be used, and are not INDs, need to be named.

Note: A protocol can be reviewed, but not approved if the IND is pending.

If a device is investigational, an IDE number should be reported in the IRB submission. It should be supported and verified in a similar fashion to an IND.

Note: A protocol can be reviewed, but not approved if the IDE is pending.

Note: If the device has HUD status, this is the wrong protocol to use, and the study needs to be sent back.

Data Protection

If there are any questions regarding the security of the data collected in this study, this should be marked with a 'yes.' If the researcher is planning to share or transfer data between institutions, it is recommended that the researcher select 'yes.'

Attachments

Any attachment noted on the Questionnaire page must be included here: Consent forms, advertisements, recruitment scripts, letters, surveys, variable lists, HIPAA forms, etc.

Any assent, consent, or parental consent must be in .pdf format in order to be watermarked. We cannot approve if not a .pdf.

All previous amendments and continuing reviews should be removed from this section, since the newest one is now in the Questionnaire section.

Note: Any non-valid attachments should be removed: such as replaced investigator brochures, questionnaires, or sponsored protocol. If the study is a migration from BRAAN, the BRAAN protocol should be left in the attachments as a reference, but not the latest BRAAN approval letter since that has been superseded by the newest KC approval.

COI forms and CITI training should also not be in this section but rather under Personnel.

Responses to the IRB should not be in this section. They should be in the Notes section of the Questionnaire tab.

Correspondence

If the submission is a revisions request, the request can be found in the Correspondence section. This allows you to look up what was requested before and the dates of actions. If this is an amendment or renewal, the History will show only the history of the current amendment/renewal.

Protocol History

If the submission is a revisions request, the request can be found in the Correspondence section under History on this page. This allows you to look up what was requested before and the dates of actions. If this is an amendment or renewal, the History will show only the history of the current submission.

Protocol Actions

The **Route Log** will show when the submission was created and when it arrived in the ORIC.

Online Review

Determination Recommendation

Something must be selected by the reviewer. The reviewers of an Expedited study should only use:

- Defer - Specific Minor Revisions: this will indicate that the protocol must be sent back to the researcher for revisions, before being approved
- Approved

Note: Defer - Substantive Revisions should only be used for Full Board/Clinical Trial studies, unless the reviewer would like to refer the protocol for full board review.

Note: No expedited reviewer may disapprove a study, only the full board can take that action. If the reviewer feels a study should be disapproved, it must be referred for full board review

Reviewer Feedback Forms (RFF)

Each of the reviewer feedback form asks questions which should help with the reviews, and serve as a guidance to what reviewers should look for when reviewing the study. The Initial Review and the CR checklists have information on the expedited categories.

- When reviewing an initial review use the Initial Protocol Checklist.
- The CR checklist is for all renewals.
- The other RFFs should be self-explanatory. (Please contact the office if further guidance is necessary)

Remember if you have already seen the protocol and it is returned for revisions review, please use the Contingent Review RFF, which is very short.

The Unanticipated Event form is the RFF for all deviations, violations, UPIRTSOs, AEs and SAEs.

Note: The Conflict of Interest RFF is mandatory for all reviews.

Comments

Each comment should be placed separately (the reason is that despite the formatting and space, when incorporated into a letter for the PI, it all comes together into one paragraph – which is very hard for the PI to read and may lead to missing some of the comments).

After writing in the comment, **always click 'add'** (button on the right). If you do not click this button, the comment will not save to the protocol.

If this is the final review and you are ready to approve either an initial protocol review or a continuing review of an expedited study, please remember to put the expedited category in the comments.

- When complete, please click the button labeled “Approve Review.”

Note: Full Board protocols are assigned to two or more reviewers. The comments from the other reviewers can be seen at the bottom of the Online Review page.