Penn
University of Pennsylvania
Human Research Protections Program

Biomedical Research
Submission Completion Guidance

What does the IRB look for when reviewing a submission? The following includes the standard completeness checks that administrators will assess about your biomedical study prior to sending it to a Board or delegated member reviewer. Please review the below questions when creating the initial submission in order to ensure that your application is complete prior to submission. ***This can reduce the number of stipulations and questions posed.***

Contents

HS-ERA Application

Basic Info Page

- Protocol Title: Confirm that the full study title in HS-ERA matches the full title in both the study protocol and the informed consent form. The IRB must have an accurate study title in the system for reporting purposes.
- Brief description of the protocol: Please provide a brief abstract about the study. *If a standalone protocol exists, you may* ***not*** *reference the protocol in this section.*
- Hospital Sites: Confirm that the hospital sites question is answered correctly. This question is important for compliance with PA Department of Health requirements and informs about satellite hospital review requirements.

Personnel Page

- Principal Investigator:
  - For *greater than minimal risk research*: Confirm that the Principal Investigator a member of Penn faculty. It is Penn policy that the PI must be a member of Penn faculty for greater than minimal risk research.
    - At satellite hospitals such as Princeton Health or Chester County hospital, confirm that the Principal Investigator is a Penn employed staff member. Unemployed individuals may not serve as the Principal Investigator. They may serve as a co-investigator under the oversight of Penn Faculty, or a Penn employed clinician, with an executed individual investigator agreement.
  - For *minimal risk research*: Confirm that the Principal Investigator is Penn Faculty, or a Penn employed staff member. *Students are not permitted to be listed as the Principal Investigator*. This is to ensure oversight over the research and that access to the protocol will always be available in case a student or an unaffiliated individual moves prior to completion of the protocol.
- Responsible Org: Ensure the responsible org is accurate. This ensures that your research is directed to the correct department chair. ***If this section shows 2100 for the health system, it must be changed as this org has no designated department chair.*** Please contact your administration or business administrator for guidance if you're unsure what to change your department chair to.
- Disclosure of Significant Financial Interests/ Penn Intellectual Property: Are there any conflicts of interest or Intellectual Property (IP) to be reported? ***If a Conflict of Interest or IP is reported, the IRB will not issue approval until we receive notice from CISC that the protocol may be approved.*** Please ensure your disclosures are submitted to avoid approval delays. Please see https://research.upenn.edu/compliance-and-training/research-integrity for guidance.
- General:
  - Confirm all study team members completed the Human Subjects' Research curriculum in CITI. If some are reflected as having incomplete training, contact them for a copy of their CITI Completion Report to upload in HSERA. If they have not completed their training, you may still submit the application, but they will not be approved to participate until their training is complete.
  - Confirm that the individual creating the application is listed as either Principal Investigator, Co-Investigator or a study contact. If not listed in one of these fields, they will not have edit access to the application post-submission.
  - Confirm that all Penn personnel who are listed in the full protocol and informed consent form also listed in the Personnel Page. ***Anyone personnel who meet the DHHS definition for 'engagement in research' must be listed on the Personnel Page in HSERA.*** This includes *anyone with access to identifiable information, anyone consenting participants, and anyone who is*

intervening or interacting with participants as part of the research protocol. If you're unsure if someone is engaged in human subjects research, please refer to the Engagement in Research Determination Form for guidance.

- If there are non-Penn personnel engaged in research on the protocol, they should seek IRB approval from their institution of affiliation. If the individual(s) are unaffiliated with an institution or the institution does not have an IRB, please refer to our guidance on Collaborative Research with External Individual Investigators. Please highlight their participation in your cover letter and include copies of their CITI completion reports and signed copies of their individual investigator agreements.

Bio /HRPP Page

Questions on this page are associated with institutional approvals and other federal, state or institutional requirements. This page also sends notifications to ancillary committees and other groups to inform them of your research.

Questions on the Bio/HRPP Page will also be checked for consistency with a standalone protocol (if applicable) and other documents submitted.

- Clinical Trial: Carefully review the NIH definition of a clinical trial embedded within the question and confirm the response is answered correctly. IRB staff will assess whether this is answered correctly and whether additional requirements apply. Guidance is available here.
- Investigator Initiated Trial: If a faculty member at Penn or another academic institution authored the protocol and it meets the FDA definition of a clinical investigation by administering a drug or investigating a device, the response to this question should be Yes.
- Drugs and Devices: If the research involves the use / administration of an FDA regulated product, the FDA regulatory pathway should be reflected here. NOTE: Research administering a drug as part of research procedures requires a standalone protocol. Additionally, a device study that is not exempt from IDE regulations requires a standalone protocol.
- Research Device Management: If your study involves the use of an investigational device, please reflect how the device will be managed. If the team is managing the device, please ensure your standalone protocol describes the device management. Please reach out to Office of Clinical Research (OCR) Compliance if you need guidance on device management.
- Drug, Herbal Product or Other Chemical Element Management: If your study involves the administration of any type of drug product (drugs, biologic, cosmetic, food, herbal supplement, etc.) as part of the research protocol procedures, please ensure your standalone protocol describes the product management. Please reach

out to Office of Clinical Research (OCR) Compliance if you need guidance on product management.

- Controlled Substance Use: If your study involves the administration of a controlled substance drug product as part of the research protocol procedures, please answer Yes and follow the associated instructions. Questions about this question should be posed to the Office of Clinical Research.
- Radiation Exposure: Are research subjects receiving radiation exposure (e.g., X-rays, DEXA scans, CT scans PET scans, etc.) that they would not receive if not enrolled in the protocol? This study will require EHRS/RRSC review to review the language & procedures surrounding radiation. If you click yes and submit the protocol via HS-ERA, they will automatically be notified about your protocol. If the ancillary committee requests any revisions to any study documentation prior to approval, please submit a modification including these requested revisions (including tracked and clean copies) to the IRB.
- Gene Transfer: If your study involves the administration of a gene therapy product as part of the research protocol procedures, please answer Yes. This study will require review and approval by the Institutional Biosafety Committee (IBC). Please note that the IRB will not issue final approval until IBC approval has been issued. A reminder of this required review will be included in the determination letter.
- CAMRIS and MRI Studies: Are research subjects receiving MRI scans that they would not receive if not enrolled in the protocol? This study will require review by the Center for Advanced Magnetic Resonance Imaging and Spectroscopy (CAMRIS).
- Cancer Related research not being conducted by an NCI cooperative group: Does this protocol involve cancer-related studies of any of the categories listed in HS-ERA? If Yes: This study will require review by CTSRMC. Please either include the CTSRMC letter of approval and any required changes or confirmation that CTSRMC review is underway in the response submission after IRB review. A reminder of this will be included in the determination letter.
- Medical Information Disclosure: Does your study involve the collection of protected health information (PHI) from the medical record or directly from the participant? Does your study involved the generation/creation of research data under a covered entity such as Penn Medicine or Penn Dental? If yes to any of these questions, HIPAA applies. Answer Yes and reflect your plan for HIPAA authorization.
- Out of State Research: If research activities are occurring at Penn Medicine sites in New Jersey, the IRB needs to assess applicable state laws.

Sponsor Page

Questions on this page are reflective of regulatory sponsorship (oversight) and funding.

- Business Administrator: Confirm that the business administrator (internal financial contact) is identified. This is important for discussions regarding any potential IRB billing concerns.

- Department budget code: Please include your budget code if the study is industry funded or a single IRB study where Penn is the IRB of Record. This is used for billing IRB fees. This information should be included at the initial submission, whether the contract is pending or not. As of May 2021, if the IRB billing office is unable to secure a budget code for the charges from the department within two months from the date of billing, they will automatically charge the department's 01XX01 Fund. It will then be the responsibility of the department to reallocate the charges to the correct sponsor project fund.
- Funding Sponsor: Please ensure this section lists the entity funding the research, if applicable.
- Regulatory Sponsor: If the regulatory sponsor of an IND or IDE protocol is an entity such as an industry sponsor, this should be reflected in this section.
- IND Sponsor: If the regulatory sponsor of an IND or IDE protocol is a Penn faculty member, this should be reflected in this section.
- Industry Sponsor: If the funding sponsor is not selectable under Funding Sponsor, please add them there for billing purposes.

Centers Page
Questions on this page are to reflect when Penn is the lead of a multicenter study and/or when Penn IRB is the IRB of Record for Multiple sites (i.e., Penn IRB is the sIRB). If Penn will serve as the IRB of Record, please ensure site information for all known relying sites is included in this section.

Protocol Page
Questions on the Protocol Page will be checked for consistency with a standalone protocol (if applicable) and other documents submitted.

Generally, if a standalone protocol exists, references may be made on this page to relevant sections of the approved protocol (e.g., Section 5.1). References should **not** be made to protocol page numbers because they change more frequently with protocol amendments. However, there are some sections where referencing the protocol is not permitted.

- Abstract: May NOT refer to the protocol, as basic information must be contained in the application for documentation purposes, and the review of subsequent submissions without an attached protocol.
- Overall Objectives: May NOT refer to the protocol, as basic information must be contained in the application for documentation purposes, and the review of subsequent submissions without an attached protocol.
- Study Duration: Confirm that the response or reference to protocol includes both 1) the expected duration of a subject's participation (from consenting to completion) as

well as 2) the expected duration of the study overall (from approval to closure) is included in the Study Duration section.

- Resources Necessary for human research protection: May NOT refer to a protocol for multicenter research as this requires a local assessment. It is a criterion for approval that the local study team have adequate resources to conduct the study to ensure the safety, rights, and welfare of participants are upheld. Confirm that you have outlined the following:
  a. Briefly describe research staff qualifications and justify that the staff are adequate in number and qualifications to conduct the research and ensure the protection of participants.
  b. Describe how you will ensure that all staff assisting with the research are adequately informed about the protocol and their research related duties. Describe plans for site initiation training as well as training if the protocol is amended.
  c. As applicable to the research, please describe the facilities available for use in the research.

Populations Page
Questions on the Populations Page will be checked for consistency with a standalone protocol (if applicable) and other documents submitted.

Generally, if a standalone protocol exists, references may be made on this page to relevant sections of the approved protocol (e.g., Section 5.1). References should **not** be made to protocol page numbers because they change more frequently with protocol amendments. However, there are some sections where referencing the protocol is not permitted.

- Target population: May NOT refer to the protocol, as basic information must be contained in the application for documentation purposes, and the review of subsequent submissions without an attached protocol.
- Subjects enrolled by Penn Researchers: Confirm that this reflects the number of participants prospectively consented; or for secondary research (e.g., chart review), confirm that it reflects the total number of charts reviewed, samples acquired, etc.
- Key Inclusion Criteria/ Key Exclusion Criteria: Confirm that the selection criteria have appropriate rationale for their inclusion. Research should not be the sole burden of specific groups of people, and groups should not be excluded without appropriate scientific or safety rationale.
  - Do the selection criteria exclude pregnant individuals? If yes:
    - Confirm that it is clear how lack of pregnancy will be confirmed. E.g., will pregnancy testing be conducted? Confirm this and the method (blood or urine) accurately reflected in the protocol and consent form.

    - Confirm whether contraception is required for participation. Confirm that the methods are accurately detailed in the protocol and consent form.
  - Do the selection criteria exclude those with infectious diseases? If yes:
    - Is infectious disease testing being performed? If yes, confirm that the necessary reporting language is included in the informed consent form.
- Vulnerable Populations:
  - Will pregnant women, fetuses, or neonates be targeted for prospective study enrollment?
    - If Yes: Please complete and upload a Subpart B form to the submission. This form is not required if the study involves secondary data use.
  - Will prisoners be targeted for enrollment?
    - Yes: Please complete and upload a Subpart C form to the submission.
  - Will children be targeted for prospective study enrollment? If yes:
    - Please complete and upload a Subpart D form to the submission. This form is not required if the study involves secondary data use.
    - Please ensure that a parental permission form and (if appropriate for the children's age range) assent form are included with the application.
- Populations vulnerable to undue influence or coercion: Please confirm that you have identified any other vulnerable populations that may be targeted for enrollment on the study such as:
  - Penn students or employees,
  - Decisionally impaired individuals,
  - Members of disenfranchised racial or ethnic communities,
  - Members of disenfranchised groups, such as the LGBTQ+ community,
  - Members of the Armed Forces and veterans,
  - Refugees, undocumented immigrants, etc.,
  - Educationally disadvantaged persons,
  - Economically disadvantaged persons,
  - Homeless persons,
  - Institutionalized individuals,

- Individuals with disabilities,
- Individuals with mental illness and/or substance use disorders

The above list may not be exhaustive. If any other vulnerable populations may be targeted for enrollment, please describe your plans for ensuring enrollment on the study will be free from undue influence.

- Subject Recruitment: A plan should be provided for any studies where there is prospective enrollment of participants. This section may NOT refer to a protocol for multicenter research. A local recruitment plan is required if recruitment is occurring locally, and the protocol is written by an industry sponsor or another site. Please ensure that the recruitment plan aligns with the IRB Guidance entitled, Recruiting Human Research Subjects: Guidance and Requirements.
- Recruitment Materials: Please ensure that the recruitment materials (advertisements, brochures, letters, broadcast materials, etc.) are uploaded and align with the IRB Guidance entitled, Recruiting Human Research Subjects: Guidance and Requirements (linked above). If your materials are not yet completed at time of initial submission (e.g., you want to recruit via flyers but haven't drafted them yet), please note that accordingly in the cover letter. As a reminder, the recruitment materials still cannot be used until submitted to and approved by the IRB.
- Compensation: If applicable to the study:
  - Confirm that you have included the amount, whether compensation will be prorated, the method of compensation and whether social security number is required for payment.
  - Confirm HSERA aligns with the consent form.
  - If social security is required for payment, please ensure this is also stated in the consent and include IRS reporting template language.

Procedures Page

Questions on the Procedures Page will be checked for consistency with a standalone protocol (if applicable) and other documents submitted.

Generally, if a standalone protocol exists, references may be made on this page to relevant sections of the approved protocol (e.g., Section 5.1). References should **not** be made to protocol page numbers because they change more frequently with protocol amendments. However, there are some sections where referencing the protocol is not permitted.

- Procedures: Research procedures should be detailed, or protocol section referenced. If the study procedures are complex with multiple study visits, it is generally recommended to refer to the protocol in this section. Uploading a table of study procedures can be useful.

- For studies involving FDA regulated products: Will data be collected in the event of an *incidental pregnancy*?
  - If Yes: Confirm the protocol and consent clearly outline whether data will be collected only on enrolled participants of childbearing potential, or also on pregnant partners of male subjects.
  - Confirm that the required materials below are uploaded with the initial submission OR include a statement in the Procedures section that the required materials will be submitted via a modification prior to data collection, should an incidental pregnancy occur. Required information and materials for data collection of incidental pregnancy:
    - Protocol/HSERA: A specification of the type of data to be collected for pregnancy follow-up
    - Protocol/HSERA: A description of how this data collection will occur
    - Main Informed Consent: A statement that the study team will request to collect data on the subject or the pregnant partner of a male subject in the event of an incidental pregnancy
    - Pregnant partner informed consent form (if data will be collected on pregnant partners)

- Analysis Plan: Confirm that HSERA or your referenced standalone protocol include a data analysis plan, including any qualitative or quantitative (e.g., descriptive, inferential, or Bayesian statistical tests) analysis to be conducted. It is important to write a statistical plan at the onset to minimize bias and to ensure sound research design.
- Subject Confidentiality: This section may NOT refer to a protocol for multicenter research. Confirm that a local plan to protect data confidentiality is detailed if the protocol is written by an industry sponsor or another site. Please ensure that the confidentiality plan aligns with the IRB Guidance entitled IRB & Penn Medicine Requirements regarding HIPAA PHI Security and Storage.
- Subject Privacy: This section does not refer to HIPAA privacy. Privacy refers to the subject's ability to control access to their person/body. Examples include consenting the subject in a private room, etc.
- Data Disclosure: This section may NOT refer to a protocol for multicenter research if the protocol is written by an industry sponsor or another site, as it should discuss sharing of data and specimens outside of the local institution. Detail disclosures of participant data and / or specimens to any external entities, regardless of level of identifiability. Confirm an agreement or contract will be executed prior to sharing data and / or specimens.

- Protected Health Information: Confirm the list of identifiers checked matches identifiers listed in the HIPAA Authorization section of the consent form or the HIPAA waiver, as applicable to your study.
- Tissue Specimens Obtained as Part of Research: If your research collects or obtains any biospecimens (blood, urine, sputum, etc.) for research purposes, confirm this is marked Yes and answer the subsequent questions.
- Genetic Testing: Genetic testing includes any analysis of human DNA, RNA, chromosomes, proteins, or metabolites, that detects genotypes, mutations, or chromosomal changes.
    - Consent Form: Confirm that the consent form includes genetic testing risks / GINA language.
    - Exploratory genetic testing: Confirm in HSERA or the referenced protocol that results will not be returned to participants.
    - Predictive genetic testing: Confirm in HSERA or the referenced protocol that a plan is outlined for disclosing results to subjects and provision of genetic counseling. Provide information on the FDA approval status of the test, which would be considered a medical device.

Consent Page
Questions on the Consent Page will be checked for consistency with a standalone protocol (if applicable) and other documents submitted.

Generally, if a standalone protocol exists, references may be made on this page to relevant sections of the approved protocol (e.g., Section 5.1). References should **not** be made to protocol page numbers because they change more frequently with protocol amendments.

- Consent Process, Overview: If you are obtaining prospective consent, confirm HSERA or the referenced protocol describes the circumstances under which consent will be sought and obtained, who will seek it, the nature of the information to be provided to prospective subjects during the consent discussion, and the method of documenting consent.
- Children and Adolescents: If you've checked that you are including children on the Populations page, confirm you have covered the following in HSERA or the referenced protocol:
    - Obtaining permission from one or both parents/legal guardian(s);
    - Obtaining assent from the child based on age/competency. It is generally considered that children aged 7-9 and older are competent to assent; and
    - Any need to re-consent children at age 18 (if long-term participation applies).

- Adult Subjects Not Competent to Give Consent: If you are including participants who may be decisionally impaired, complete the Research Involving Cognitively Impaired Adults Supplemental Form.
- Waiver of Consent:
  - If you are requesting a full waiver of informed consent, confirm you have selected *Waiver or alteration of required elements of consent* and provide rationale for waiving informed consent.
  - If you are requesting a waiver of documentation of consent for verbal or electronic consent processes, confirm you have selected either of the following, as applicable:
    - *Waiver of written documentation of informed consent: the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality.*
    - *Waiver of written documentation of informed consent: the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context*

Risk Benefit Page
Questions on the Risk Benefit Page will be checked for consistency with a standalone protocol (if applicable) and other documents submitted.

Generally, if a standalone protocol exists, references may be made on this page to relevant sections of the approved protocol (e.g., Section 5.1). References should **not** be made to protocol page numbers because they change more frequently with protocol amendments. However, there are some sections where referencing the protocol is not permitted.

- Potential Study Risks: This section may NOT refer to a protocol or a consent form for documentation purposes, and the review of subsequent submissions without an attached protocol. Confirm that the study risks are outlined in this section. It is recommended that this be copied and pasted from the consent form. It should be kept updated with subsequent modifications.
- Potential Study Benefits: This section may NOT refer to a protocol or a consent form for documentation purposes, and the review of subsequent submissions without an attached protocol. Confirm that the potential benefits to participants are outlined in this section.
- Data and Safety Monitoring: If the study is greater than minimal risk, confirm that a Data and Safety Monitoring Plan (DSMP) is outlined in HSERA or the referenced protocol. A DSMP should be designed based on complexity and risk of the protocol.

- Research that is **minimal risk** usually does not require a DSMP, with most exceptions falling under expedited category 1 involving drugs and devices. For all minimal risk research, there should be clear methods to protect confidentiality and privacy as well as subject safety that are commensurate with the risk.

For additional guidance, please review the IRB's guidance on Data and Safety Monitoring Plans (DSMP).

Confirmation Page – Document Upload Check
This is where you should upload documents associated with the research study.

Completeness Check	Yes	No	Confirmation
Is the HS-ERA online application meant to serve as the full protocol?	☐	☐	If NO: Confirm a full protocol standalone is uploaded.
Is the study obtaining prospective informed consent?	☐	☐	If YES: ○ ☐ Confirm all study Informed Consent/ Assent/ Parental Permission Forms are uploaded when *consent will be documented.* ○ ☐ Confirm consent script or information sheet is uploaded *if verbal or phone consent is being obtained.* ○ ☐ If the study is being conducted under the Penn Medicine or Penn Dental covered entity, confirm your consent form contains HIPAA Authorization language (*Penn Medicine template authorization is part of the Biomedical Consent Form Template; template Penn Dental authorization language is available on the forms page*)
Are you are requesting a waiver of HIPAA authorization [*for research that involves accessing (using), collecting, and/or disclosing (sharing) protected health information (PHI)*]?	☐	☐	If YES: Confirm you have uploaded the Request for a Waiver of HIPAA Authorization Form.
Are drug products being administered for research purposes? For guidance, please see Research with Drug Products.	☐	☐	If YES: ○ ☐ Confirm a full standalone protocol is uploaded. HSERA may not serve as the IRB protocol. Templates are available on the IRB Forms page. ○ ☐ Upload a copy of documentation of your IND from the FDA, or IND exemption from Penn Medicine OCR, the FDA, or other internal entity, if available. If requesting the IRB determine IND exemption (non-Penn Medicine research), confirm

Completeness Check	Yes	No	Confirmation
			the Research with Drugs supplemental form is uploaded. ○ ☐ Confirm the Investigator's Brochure OR Package Insert for the product containing reference safety information is uploaded.
Is a device being investigated under an abbreviated IDE (non-significant risk) or full IDE (significant risk)? For guidance, please see Research with Device Products.	☐	☐	If YES: ○ ☐ Confirm a full standalone protocol is uploaded. HSERA may not serve as the IRB protocol. Templates are available on the IRB Forms page. ○ ☐ Confirm the Device Brochure for the product containing reference safety information is uploaded. ○ ☐ Confirm that the Investigational Plan is either uploaded OR part of the protocol. ○ ☐ If Non-Significant Risk: Confirm the Research with Devices supplemental form is uploaded so that the IRB may assess the rationale for the risk level of the device as used on the protocol. ○ ☐ If Significant Risk: Upload FDA approval of the IDE.
Will the study involve any questionnaires, inventories, surveys, diaries, personality tests, quality of life assessments, data collection forms, or interviews?	☐	☐	If YES: ○ If validated and widely recognized/ accepted: confirm the protocol describes their use. ○ If not validated, nor widely recognized/ accepted (i.e., developed for the purposes of the study): confirm they are uploaded. *NOTE: If you have multiple of these types of documents, please consider combining into 1 PDF as opposed to uploading each document separately to facilitate IRB review.*
Will the study involve using recruitment materials (e.g., brochures, flyers, videos, scripts for radio advertisements, etc.)?	☐	☐	If YES: Confirm they are uploaded and align with the IRB Guidance Recruiting Human Research Subjects: Guidance and Requirements.

Completeness Check	Yes	No	Confirmation
Will you present any other documentation to participants (participant facing materials)?	☐	☐	If YES: Confirm they are uploaded.
Are you working with a community partner to execute the research?	☐	☐	If YES: ○ Confirm the Community Based Research supplemental form is uploaded. ○ Confirm a letter of support from the site is uploaded.
Is the study funded by any of the following entities: Department of Defense Department of Education Department of Energy Department of Justice Environmental Protection Agency (EPA)	☐	☐	If YES: Confirm the associated supplemental form is uploaded.
Is Penn serving as the IRB of Record for other institutions?	☐	☐	If YES: ○ Confirm you have discussed Penn serving as the sIRB with the Reliance Manager ○ Confirm the Centers page is complete. ○ If the IRB needs to sign an IRB Authorization Agreement, confirm it is uploaded.
Review the personnel page. Are any personnel shown as missing CITI training?	☐	☐	If YES: ○ If completed: Obtain their certificate of completion ○ If incomplete: Notify them to complete their training and continue with submission.