

UNIVERSITY
OF MINNESOTA
Driven to DiscoverSM

Investigator Manual (HRP-103)

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Investigator Manual Revision History

Version	Version Date	Summary of Changes
1	March 27, 2017	N/A.
2	July 21, 2017	Updated information regarding training, case studies, research with data or specimens, research with controlled substances, disagreement with the IRB's determination, submission of reportable new information, suspended or terminated research
3	September 15, 2017	Updated information about reportable new information, scientific assessment
4	January 18, 2018	Revised to reflect NIH Single IRB Review Policy requirements, clarification of advisor availability, monitoring report process, and expectations for complaints and concerns.
5	March 26, 2018	Revised reportable new information guidance, education requirements for Fairview, Gillette, and UMP employees, PI eligibility for UMP employees, requirements for changes to exempt and not human research studies, clarified protocol format requirements, added instructions for transferring PI responsibilities, clarified COC guidance, added fetal tissue procedures, added external IRB standard consent language links, added translation and certification resources, and added HRPP Central File policy link.
6	April 30, 2018	Clarified the letter requirements for 'Who may be the principal investigator for Human Research?' to include Center Director; Clarified exception to protocol WORD version requirement, including process guidance; Added data security guidance provided by University Information Security; Added Gillette Children's Specialty Healthcare Scientific Review as an acceptable method for scientific assessment; clarified exempt vs. non-exempt translation/certification requirements; clarified meaning of enrollment for continuing review submissions; removed 'Review Fee for Business- and Industry-Sponsored Projects Reviewed by Quorum IRB'
7	May 29, 2018	Added regulatory information about IRB reporting obligations, removed pre-ETHOS submission prompt reporting instructions for validation submissions, added Click Translations Service for certificates of translation, added participant education materials information, clarified IRB submission requirements for studies involving adults with impaired decision-making capacity, added guidance for studies involving non-English speaking adults with impaired decision-making capacity
8	June 25, 2018	Added "HRP-574: Certification Attestation of Translation" template reference and guidance for use for studies requiring certification of translated study materials; Added additional guidance related to IRB's role in the receipt of sponsor communications such as Medical Device Reports to the RNI section; Clarified University requirements for consent template language for studies where the sponsor has developed the consent document; Updated Toolkit reference

		for the External Team Member form from HRP-212 to HRP-216.
9	December 1, 2018	Revisions to remove specific reference to Quorum Review IRB for external IRB reliance for B & I studies. Include use of other commercial/independent IRBs permitted where UMN has a master agreement in places with that commercial/independent IRB (e.g., Quorum and Advarra). Updated CoC Assurance Letter request instructions. Replaced the name of the Post Approval Review Program (PAR) with Quality Assurance Program. Added 45-day response requirement.
10	January 14, 2019	Added GDPR requirements, Updated IRB Office address, Added requirement to upload track-change copies of modified documents under “How do I submit a Modification?” Added reference to “IRB Review of Conflicts of Interest (HRP-054)”, Updated Associate VP for Research contact information for PI eligibility requests, Clarified the IRB Fee requirements as it relates to IRB approval, removed duplicative information regarding expanded access and included references to applicable worksheets, added information regarding continuing review requirements under the Revised Common Rule.
11	February 28, 2019	Added information about what types of projects may not require IRB review, added question and response for the difference between quality improvement activities and research, renamed Site Supplement to Local Protocol Addendum (HRP-508), combined responses related to continuing review submissions into one question, added Librarian job codes for PI eligibility, added guidance about research involving foster children, added Appendix B-1 regarding parental consent requirements for research involving children, clarified time sensitive matter submissions and modifications that require a new IRB submission, added guidance about the completion of continuing review form questions related to enrollment.
12	April 30, 2019	Added guidance about recruitment methods and research involving students. Updated guidance and instructions for research involving human fetal tissue and potentially hazardous biological agents including human gene transfer. Added requirements for research using the short form method of consent, added guidance about the involvement of interpreters, added guidance regarding significant new findings and re-consent, added new process for HRPP Scientific Assessment in ETHOS
13	August 1, 2019	Fixed formatting of bullets, headings, grammar, and ‘Return to Table of Contents.’ Added guidance about the development of a repository, database, or registry, Added guidance about existing repositories and regulatory compliance

		<p>Added guidance about what data / specimen activities require IRB review, including secondary use, collection, and sharing of</p> <p>Added IRB and HIPAA applicability matrix for data / specimen related research in Appendix B-2</p> <p>Clarified the scope of a quality improvement registry / database</p> <p>Added decision tree for prompt reporting in Appendix B-3</p> <p>clarified the timing for review of fetal tissue research, and clarified research record retention, added reference to UMN policy about record retention,</p> <p>added guidance about tele-consent, e-consent, mail consent, electronic signatures, electronic storage of study documents.</p> <p>Added guidance about research where the University of Minnesota is serving only as the coordinating center for a study</p> <p>Added references to new Registry/Database/Repository protocol (HRP-597) and HUD protocol (HRP-591).</p> <p>Clarified Just-in-Time submission process</p> <p>Added guidance about the use of volunteers or “Temp/Casual” staff as study personnel.</p> <p>Updated references to standard consent language templates, removing Quorum IRB review references.</p> <p>Revised guidance regarding Non-Significant Risk and Significant Risk Determinations</p> <p>Replaced HRPP Scientific Assessment instructions for the Portal with ETHOS instructions</p> <p>Added guidance about long term follow-up for human gene therapy studies</p> <p>Clarified fetal tissue research review process</p> <p>Added ancillary review obligations for when relying on an external IRB</p> <p>Clarified individual patient expanded access IND guidelines from NIH to include emergency access</p> <p>Revised the instructions on how to close a study with the IRB</p>
14	January 17, 2020	Updated content to reflect updated Toolkit numbered documents related to reliance, added single IRB (sIRB) review information to comply with 2018 Rule requirements.
15	May 15, 2020	Updated content related to electronic consent and Part 11 compliance. Clarified process for PI attendance at panel meetings. Updated reliance toolkit references for HRP-228 and HRP-831. Updated content related to research participant educational resources.
16	January 6, 2020	<p>Removed the question, “Can I use the short form method more than once for a non-English speaker?” as the guidance was outdated.</p> <p>Clarified and expanded guidance for the question, “What is required after obtaining consent using the short form method?”</p>

		<p>Clarified requirements for use of a standalone HIPAA authorization for research involving non-English speaking participants.</p> <p>Added Appendix B-4 which includes clarifications regarding short form and consent translation requirements.</p> <p>Added guidance regarding exceptions to PI eligibility criteria.</p> <p>Clarified B&I fee applicability to apply to studies that are greater than minimal risk.</p> <p>Clarified student-investigator submission process for “What if I’m teaching a research methods or “courseroom” class?”</p> <p>Corrected Toolkit reference errors for HRP-591, HRP-595, and HRP-410.</p> <p>Removed outdated guidance regarding the UMN IRB ability to serve as sIRB.</p> <p>Updated the process for IRB review of human research where an Institutional Conflicts of Interest exists to align with HRP-054.</p>
17	March 31, 2021	<p>Addressed minor spelling or grammatical errors.</p> <p>Added additional guidance regarding the addition of study personnel to IRB approved submissions (see “Who is considered Study Personnel for purposes of IRB submission?”).</p> <p>Added new guidance regarding participant compensation (see “How do I develop a compensation plan for research participation?”).</p> <p>Added guidance regarding the use of ETHOS to obtain the IRB approved consent form (see “How do I create a consent document?”).</p> <p>Added guidance regarding HUD submission review to “Does my research require scientific assessment?”</p> <p>Removed “Clinical and Translational Science Institute (CTSI) pilot funding awards” from “Does my research require scientific assessment?”</p> <p>Revised guidance regarding Just-In-Time submissions (see “What if I applied for federal funding and received a Just-in-Time notification?”).</p> <p>Added guidance regarding research involving children (see “What if I’m doing research involving children?”).</p> <p>Added information regarding expectations for responding to requests from the IRB within 45 days of notices being sent (see “What will happen after IRB review?”).</p> <p>Added modification submission guidance regarding the addition of study personnel to existing protocols who plan to conduct a research study using the existing study</p>

		<p>data/specimens (see “How will the modification be reviewed?”).</p> <p>Added instructions regarding the requirement to submit reportable new information at the time of continuing review in the event of a lapsed IRB approval (see “How do I submit continuing review?”).</p> <p>Added non-compliance statement to “How do I close out a study?”</p> <p>Added “Can I be restricted from submitting to the IRB?”</p> <p>Added prompt reporting of a death of a local research participant to reporting requirements for research being reviewed by an external IRB (see “What do I submit to the University of Minnesota IRB after my study is approved for reliance on an External IRB?”).</p> <p>Removed exception request process for reliance on an external IRB and replaced with a new process for appealing decisions to not allow reliance (see “</p> <p>Added appeal process for situations where UMN IRB declines to serve as sIRB or declines a request to rely on an external IRB (see “How do I request the University of Minnesota serve as the sIRB?” and “How do I know my study is eligible for reliance on an external IRB?”).</p> <p>Clarified process information for sIRB requests (see “How do I request the University of Minnesota serve as the sIRB?”).</p> <p>Updated process for requesting reliance on an external IRB (see “What is the process for requesting reliance on an external IRB?”)</p> <p>Removed IND/IDE Regulatory Director references.</p> <p>Addressed minor spelling/grammar issues.</p> <p>Revised Appendix B-1 Research Involving Children to align with new guidance from the Office of the General Counsel.</p>
18	June 1, 2021	<p>Revised guidance (content and organization of content) related to reliance on an external IRB and requests for UMN IRB to serve as sIRB (pp. 75-81);</p> <p>Added instructions on how to request reliance in ETHOS;</p> <p>Clarified guidance on submitting updates related to reliance submissions;</p> <p>Added Appendix B-5: Examples for sIRB, Reliance on an External IRB, Individual Investigator Authorization Agreements</p> <p>Added references to WORKSHEET: Local Context Review for Relying on an External IRB (HRP-830), WORKSHEET: Individual Investigator Authorization Agreements (HRP-832), FORM: PI Attestation Form for UMN IRB to Serve as sIRB (HRP-828), and FORM: PI Attestation Form for Reliance on an External IRB (HRP-829);</p> <p>Added “yes/no” to the Appendix B-1 decision tree;</p> <p>Added “Can the IRB issue retrospective approval of research I have already conducted?”</p> <p>Added “What are the consequences of conducting human subjects research without prior IRB approval?”</p>

19	November 1, 2021	<p>Fixed broken and missing hyperlinks;</p> <p>Clarified PI eligibility for faculty with emeritus status or who are tenured and retired;</p> <p>Addressed minor formatting, spelling and grammatical errors;</p> <p>Clarified when sub-projects should be submitted as a separate protocol;</p> <p>Clarified that study related materials (i.e. Instruments, tests, surveys, and recruitment material) should not be appended to the study protocol but uploaded separately in ETHOS;</p> <p>Revised guidance for participant compensation;</p> <p>Clarified the submission process for electronic consent;</p> <p>Clarified processes and applicability of the Certificate of Confidentiality (CoC);</p> <p>Clarified requirements and limitations of consent for research involving children;</p> <p>Changed subject to participant;</p> <p>Added information about translated versions of the HIPAA Authorization Form;</p> <p>Clarified policy for Using Legend and Investigational Drugs for Clinical Research and Fairview IDS identification;</p> <p>Added Section “Does the IRB have guidelines regarding risk levels of common research related medical procedures?”;</p> <p>Clarified guidance on using IRB approved-stamped consent form;</p> <p>Provided guidance regarding title changes associated with new funding, frequent changes in personnel and funding changes;</p> <p>Clarified RNIs for changes that significantly affect research conduct but are outside the investigator’s control;</p> <p>Added requirement for Federalwide Assurance for Entities Collaborating or Participating in the Conduct of Research for which the U of M is the IRB of Record;</p> <p>Updated Appendix A-4 for research involving large scale genomic data (LSGD) collected on DOD-affiliated personnel;</p> <p>Updated Appendix A-5 with additional requirements for Department of Energy (DOE) Research;</p> <p>Updated Appendix A-6 with additional requirements for Department of Justice (DOJ) Research funded by the National Institute of Justice;</p> <p>Updated Appendix B-1 to align with revisions to HRP-013;</p>
20	March 31, 2022	<p>Added “How do I protect the privacy of research participants when using Zoom or other video conferencing tools?”</p> <p>Added “If re-consent is required, do I have to translate the revised study consent form?”</p> <p>Corrected typos and added “or due to safety measures related to a pandemic, natural disaster, or time of national emergencies” to “When informed consent is obtained using the ‘short form’ written consent document, can the interpreter interpret by phone or videoconference?”</p>

		<p>Provided a link to translated HIPAA forms in the “How do I obtain HIPAA Authorization for non-English speaking participants?” Deleted references to HRP542b and HRP-542c.</p> <p>Added exercise category to “Does the IRB have guidelines regarding risk levels of common research related medical or physical procedures?”</p> <p>Added “What does the IRB consider when conducting a continuing review?”</p> <p>Revised time frame for researchers to respond to the IRB from 45 to 30 days.</p> <p>Added guidance regarding requests for extension including that additional requests for extension will only be considered with approval of the research dean, and that deferrals should follow these extension guidelines.</p> <p>Added “What does the IRB consider when conducting a continuing review?”</p> <p>Removed “Circumstances that require a new IRB submission” from the Modification Review Table and Added to “Circumstances that would require submission of a new IRB application?”</p> <p>Added “Will the UMN IRB serve as the sIRB for SBIR/STTR Human Research?”</p> <p>Clarified that prompt reporting should be for an unexpected death.</p> <p>Fixed broken and missing hyperlinks due to Google Security Update in Summer 2021.</p> <p>Corrected typos.</p> <p>Replaced subject with participant.</p> <p>Replaced Research Compliance Office with Research Intelligence and Compliance Team (RIACT)</p>
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What is the purpose of this manual?

The “INVESTIGATOR MANUAL (HRP-103)” is designed to guide you through policies, procedures, and resources related to the conduct of Human Research that are specific to the University of Minnesota (“University”).

Along with this manual, current Human Research-related policies, SOPs, Worksheets, Checklists and templates may be found in the [HRPP Toolkit Library](#). Collectively, the Toolkit Library creates a complete picture of Human Research Protection Program (“HRPP”) and Institutional Review Board (“IRB”) expectations and a guide to seeking IRB review and approval. The Toolkit is also used by HRPP staff and IRB members to enhance compliance with federal, state and local requirements for conducting research and protecting human participants.

As you read through this manual and supporting documents, you may find the definitions and descriptions in “[SOP: Definitions \(HRP-001\)](#)” particularly helpful.

The University has implemented (in March 2017) the Ethical Oversight Submission System (ETHOS), a web-based platform for IRB submissions and HRPP oversight. Information about this system can be found on the [ETHOS](#) web page; job aides for use of the system can be found on the [Training and Resources](#) web page.

To ensure you are always referencing the most current version of Toolkit and related documents, please access them in real time from the IRB website rather than downloading and storing them on your computer.

We encourage you to use all of these resources to aid in the successful submission and conduct of your research study.

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Conducting Human Research at the University of Minnesota

What is Human Research?

The “[HUMAN RESEARCH PROTECTION PROGRAM PLAN \(HRP-101\)](#)” defines the activities that the University considers to be “Human Research.” An algorithm for determining whether an activity is Human Research can be found in the “[WORKSHEET: Human Research \(HRP-310\)](#)”. Use this document for guidance as to whether an activity meets either the Department of Health and Human Services (“DHHS”) or Food and Drug Association (“FDA”) definition of Human Research, keeping in mind that the IRB makes the ultimate determination in questionable cases as to whether an activity constitutes Human Research subject to IRB oversight.

With respect to research activity at the University:

1. You are responsible for following all IRB requirements for Human Research;
2. You may not conduct Human Research without prior IRB review and approval. The IRB will not review or approve research activity that has already occurred.
3. If you have questions about whether an activity is Human Research, see “[Human Research Determination Form \(HRP-503\)](#)”;
4. See “[WORKSHEET: Exemption Determination \(HRP-312\)](#)” for activities that are exempt from IRB oversight. Note that you must still submit the study to the IRB for review and an exempt determination; and
5. Human Research may be reviewed and approved by an external IRB in certain situations. See the section of this manual titled “[How do I request reliance on an external IRB?](#)” for questions regarding study eligibility and process.

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What is the Human Research Protection Program (HRPP)?

The “[HUMAN RESEARCH PROTECTION PROGRAM PLAN \(HRP-101\)](#)” describes the University’s overall plan to protect participants in Human Research. It includes:

- The mission of the Human Research Protection Program;
- The ethical principles that the University follows governing the conduct of Human Research;
- The applicable laws that govern Human Research (see also [HRP-112 for Minnesota laws](#));
- When the University becomes “engaged in Human Research” and when someone is acting as an agent of the University conducting Human Research;
- The types of Human Research that may not be conducted; and
- The roles and responsibilities of individuals within the University.

Visit the [Human Research Protection Program website](#) to learn more about the HRPP.

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Who may be the principal investigator for Human Research?

Every research study requires a Principal Investigator (PI). This person takes full responsibility for the conduct of the study. Below is a list of who may and may not serve as PI on submissions to the IRB, though unique

circumstances (e.g., requests from staff) may be given special consideration. These requirements are applied to submissions received by the IRB but do not extend institution-wide.

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University of Minnesota Affiliated

Eligible to Serve as PI:

1. Non-tenure-track research and/or clinical faculty (full, associate, and assistant professors);
2. Tenure-track faculty (full, associate, and assistant professors); and
3. Professional and Academic (P & A) employees in the following classifications: 9341A3, 9341D1, 9341D2, 9341S3, 9342K3, 9342M3, 9342M4, 9354D1, 9354M2, 9354M3, 9363M2, 9702, 9714, 9715S1, 9715S2, 9724M2, 9742N2, 9742R5, 9742R6, 9742R7, 9742S2, 9742S3, 9745S2, 9745S3, 9745S4; and
4. Associate University Librarians (9363D2), Assistant Librarian (9715), Associate Librarian (9714) and Librarian (9713)

Eligibility Determined on a Case-by-Case Basis:

- a. Other academic employees, such as P&A employees in classifications other than those listed above;
- b. Individuals with graduate student/professional training status (including medical residents and postdoctoral fellows);
- c. Employees with non-academic titles, in unusual circumstances;
- d. Faculty with emeritus status or who are tenured and retired;
- e. Adjuncts;
- f. Lecturers;
- g. Contributed Services Faculty;
- h. Health System Clinicians;
- i. Visiting faculty; and
- j. Visiting scholars.

In general, exceptions will be granted to persons in these employee categories who propose minimal risk research. Persons in these employee categories who propose to do greater than minimal risk research may serve as a member of the study team, such as co-PI, but an eligible PI is required for this risk category. In general, exceptions allowing persons in these employee categories to serve as the PI will not be granted.

Contact the Associate Vice President for Research via email (oakes007@umn.edu) to request permission. Please include:

- your CV;
- a copy of your protocol; and
- a letter of support from your Department Chair/Division Chief/Center Director; or
- a letter of support from your advisor (for individuals with graduate student/professional training status).

If approval is granted, upload the confirmation email into the “Supporting Documents” section in your ETHOS submission.

Not Eligible to Serve as PI:

1. Undergraduate students

Fairview Affiliated

- Fairview employee;
- Non-University employee with Fairview medical staff privileges;
- Persons with another affiliation with Fairview subject to Fairview authority and who is using Fairview facilities, Fairview patients in their capacity as Fairview patients, or other Fairview resources.

Fairview will institute a process whereby non-University investigators involved in research obtain from Fairview confirmation of their status as a Fairview employee or other Fairview affiliated researchers subject to Fairview authority. Upload your confirmation into the “Supporting Documents” section in your ETHOS submission. Contact Fairview Research Administration at Research@Fairview.org to request PI approval.

Gillette Affiliated

The Principal Investigator (PI) is a Gillette employed or contracted individual designated by an institution to have the appropriate level of authority and responsibility to direct a research activity. A PI must be qualified by education, training and experience in the area in which the research is being conducted.

Contact Joyce Trost via Research@gillettechildrens.com to request PI approval for your study at the same time as you request Scientific Review. Please include your CV and a copy of your protocol.

If approval is granted, confirmation of PI approval will be included in a letter that will also include scientific review approval. Upload the approval letter into the “Supporting Documents” section in your ETHOS submission.

UMP Affiliated

In order to serve as a principal investigator on a UMN human research study, the UMP physician must also hold a faculty appointment at the University of Minnesota. Under this dual-appointment, the physician must adhere to responsibilities, including but not limited to, those described in the [UMP agreement](#), University’s [HRPP Manual \(HRP-101\)](#) and Investigator Manual (HRP-103). The University PI is responsible for assuring that all members of the research team, including UMP employees, comply with all laws, regulations, standards and requirements that govern research studies and clinical trials.

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How do I transfer responsibility to a new principal investigator?

Changes of PI often prompt changes to other parts of the study. Review all consent/assent forms, recruitment materials and other documents to make certain they have been updated to reflect the change. The current PI may transfer responsibility to a new PI by creating a Modification in ETHOS and selecting “Other parts of the study” as the modification scope. This will “unlock” the section of the application that will allow you to update the PI and any other related study materials. The current PI must submit the modification. The new PI will be able to submit after the modification has been review and approved by the IRB.

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What happens if the principal investigator abruptly goes on leave or departs the institution without transferring responsibility for his or her studies?

Not all transitions can be anticipated. If a PI goes on an unanticipated leave or there is an abrupt departure from the University or one of our affiliated institutions, follow the steps below to request changing the PI.

- The department head/division chief prepares a letter on official letterhead to the IRB explaining the circumstances of the leave, identifying the current PI and study number, and naming the new PI.
- A current member of the study team prepares the modification in ETHOS to change the PI and update, as needed, any study documents (see job aid “How to submit a modification” for detailed instructions). A study team member will be able to complete all necessary steps except submitting to the IRB.
- Email the IRB at irb@umn.edu. The email must include the Modification number associated with the request to change PI and the letter from the department head. Once the request is received, IRB staff will submit the Modification on the behalf of the new PI for review. IRB staff will add a comment in the system to notify the Primary Contact that the modification was submitted. If the study does not include additional staff members or a primary contact, please contact the IRB. Please note that this process is only for use when the PI’s departure is both sudden and unanticipated.
- If there is no appropriate replacement for the PI and the department wishes to close the study, a member of the study team may complete the closure request. Upload with the submission a letter from the department head indicating the PI is no longer affiliated with the University of Minnesota, the study activities are complete, and the study should be closed. Email irb@umn.edu with the submission number and a request for the IRB staff to administratively submit.

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What if I’m a Student-Investigator?

In order to ensure adequate oversight of student-led research, your advisor is required to submit your IRB application (including Determination Forms) and any subsequent changes made to that application. You have the ability to create a study in ETHOS. You must assign your advisor to the PI/Advisor role in the ETHOS SmartForm for it to be submitted for review. For information about submitting your study, refer to the [ETHOS Guide for Students and Advisors](#) located on the IRB website.

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Advisor Role & Responsibilities

As an advisor, you are ultimately responsible for the conduct of research initiated by your student-advisee. To serve as a PI/Advisor on a student submission, you must meet the eligibility requirements of a principal investigator (See “[Who may be a principal investigator?](#)”). In submitting the study in ETHOS, you assure the IRB of the following:

1. You will assume the responsibilities required to oversee the conduct of the research, prevent harms and foster benefit to participants;
2. Any changes in the research project, adverse events, or incidents which may affect the conduct of research will be reported to the IRB;
3. You have thoroughly reviewed the proposed research study;
4. The topic and design of the study are appropriate for student research;
5. The student-investigator has the necessary experience and training to conduct the research;
6. You will meet with the student-investigator on a regular basis to monitor study progress; If the study procedures are carried out in a location away from the University or regular channels of communication are not feasible, you will make alternate arrangements to continue communication with the student-investigator;
7. The student-investigator will promptly report, and you will submit, unanticipated problems to the IRB;
8. The student-investigator will adhere to all requirements for continuing review;
9. If the student-investigator leaves the University, you will provide all necessary documents for terminating the study or continuing review; and

10. If you will be unavailable, you will arrange for an alternate faculty advisor to assume the above responsibilities and will advise the IRB of this change.

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What training is required to conduct Human Research?

Training requirements are described in “[SOP: Human Research Education and Training \(HRP-066\)](#).” All members of the research team listed on an IRB submission classified as exempt or non-exempt research, must complete the required training described in the SOP. Trainings completed at other institutions are generally not accepted. Although recommended, research team members listed on submissions determined “Not Human Research” will not be required to complete the IRB training requirements.

All members of the research team involved in the design, conduct, or reporting of the research must complete training. Members of the research team who have not completed human research protections training may not take part in aspects of the research that involve human subjects. All required training must be completed before IRB final approval can be granted. Instructions on how to complete the training requirements can be found on the [Training section](#) of the IRB website.

Fairview Affiliated

Fairview employees listed as research staff or principal investigator on a UMN human research study, must comply with UMN IRB training requirements as described in “[SOP: Human Research Education and Training \(HRP-066\)](#).” Fairview Research Administration will confirm training completions outside of UMN offerings, including Fairview’s HIPAA training.

Gillette Affiliated

Gillette employees listed as research staff or principal investigator on a UMN human research study, must comply with UMN IRB training requirements as described in “[SOP: Human Research Education and Training \(HRP-066\)](#).” Gillette will confirm training completions outside of UMN offerings, including Gillette’s HIPAA training.

UMP Affiliated

UMP employees, other than physicians, listed as research staff or principal investigator on a UMN human research study, must comply with UMN IRB training requirements as described in “[SOP: Human Research Education and Training \(HRP-066\)](#)” including the University’s HIPAA training, HIPAA19, available in the Training Hub per the [UMP agreement](#).

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How do investigators and other study personnel disclose potential conflicts of interest?

Investigators and study personnel working with human participants must follow their home institution’s policies and procedures for reporting and management of potential conflicts of interest. The IRB will make the ultimate determination as to if and how a conflict of interest can be managed to protect participants in the research.

The existence of financial and/or business interests related to the research study must be disclosed in the New Study and Continuing Review forms in ETHOS for all study personnel.

All conflicts and should be reported and resolved prior to submission to the IRB. Unresolved conflict of interest disclosures will result in a HOLD being placed on new study submissions; review will not occur until a

determination is received from the applicable oversight body above. You should upload the determination and any management plan in the Supporting Documents section of ETHOS.

Any conflict not previously disclosed to the IRB should be reported via the Reportable New Information SmartForm in ETHOS. The investigator should also submit a modification in ETHOS to address any revisions to the study as required.

The conflict determination and/or management plan will be reviewed by the convened IRB or assigned designated reviewer, depending upon the level of review required for the study. See “[IRB Review of Conflicts of Interest \(HRP-054\)](#).”

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Individual Conflicts of Interest - University of Minnesota Affiliated

For University investigators, you must disclose all reportable conflicts to the University’s [Office of Institutional Compliance](#) (OIC).

In January 2018, the University of Minnesota adopted a new financial interest policy, titled “Individual Conflict of Interest and Standards Governing Relationships with Business Entities. See <https://policy.umn.edu/operations/conflictinterest> for policy details. You are responsible for understanding and complying with the new policy.

For questions, contact Jon Guden, Associate Director of the Conflict of Interest Program, at jguden@umn.edu, or (612) 626-4727.

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Individual Conflicts of Interest - Fairview Affiliated

For Fairview investigators, conflict of interest disclosures are initially due prior to federal grant or IRB submission, and renewed by the first of each year. Disclosures must be updated at the time of change in institutional responsibilities or financial or business interests as well.

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Individual Conflicts of Interest - Gillette Affiliated

Gillette investigators must report any or all significant financial interests through completing a Financial Disclosure for Research Form (or similar form) at the start of their research involvement at Gillette Children’s and then annually thereafter and submit to Research Administration. If they, their spouse or domestic partner, or dependent children have consulting arrangements, significant financial interests, or employment in an outside entity as described above, that may affect the research endeavor that they will be pursuing, then a management plan must be created by the Research Committee or designated subcommittee. Common sense must prevail in the interpretation of these provisions. That is, if a reasonable person would question the relationship, it should be disclosed and approval sought for the proposed arrangement.

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Institutional Conflicts of Interest

The potential for institutional conflict of interest exists where the University has a significant financial interest in the research under review. If an institutional conflict of interest exists, the UMN IRB will require reliance on a commercial IRB (Advarra IRB) for human research. You must provide the IRB with any determination or management plan prior to review (for new studies) or once received for ongoing studies. The external IRB will

review the information and make a final determination as to if and how the conflict of interest can be managed to protect participants in the research. See “[IRB Review of Conflicts of Interest \(HRP-054\)](#).”

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Submitting Your Study for Review

What if I'm not sure my project requires IRB review?

The IRB reviews all activities that meet the federal definition of human research. If you are unsure if your proposed project meets that definition, refer to the “[WORKSHEET: Human Research \(HRP-310\)](#)” for guidance. The following are examples of activities that are likely not to be human research:

- Umbrella grants, training grants, and Just-in-Time grants: Requesting the IRB’s acknowledgment of receipt and “proof of concept.” These types of submissions do not include all elements required in order to obtain full IRB approval.
- Program Evaluation/Quality Assurance Review/Quality Improvement Projects: The activity is limited to program evaluation, quality assurance, or quality improvement activities designed specifically to evaluate, assure, or improve performance within a department, classroom, or hospital setting. There is no intent to alter or control the evaluation for research purposes.
- Case Report: The project consists of a case report or series (1-3 patients) which describes an interesting treatment, presentation, or outcome and is not subject to the jurisdiction of the FDA. A critical component is that nothing was done to the patient(s) with prior “research” intent. Note that HIPAA or other state or local laws may still apply to this activity. Please consult the entity from which you received or accessed the information contained in the report for further guidance.
- Course-Related Activity: The project is limited to one or more course-related activities designed specifically for educational or teaching purposes where data are collected from and about students as part of routine class exercises or assignments and otherwise do not meet either of the definitions of Human Research in Section 1.0. Note that some course-related activities, even those conducted by students, may yield information suggesting additional investigation or analysis. If an additional activity entails Human Research, then it must be submitted to the IRB for review.
- Journalistic or Documentary Activity (including Oral History): The activity is limited to investigations or interviews (structured or open-ended) that focus on specific events (current or historical), views, etc. Such investigations or interviews may be reported or published in any medium, e.g., print newspaper, documentary video, online magazine.
- Research not subject to the jurisdiction of the FDA Using Public or Non-Identifiable Private Information about Living Individuals: The activity is limited to analyzing data about living individuals (1) where the data have been retrieved by the investigator from public, non-restricted data sets or (2) where the private data have been provided to the investigator without any accompanying information by which the investigator could identify the individuals. Note that “de-identified data” according to HIPAA may be identifiable according to the DHHS definition of “Human Subjects” above. Please consult “[WORKSHEET: Human Research Determination \(HRP-310\)](#)” for clarification and contact the IRB with any questions regarding research with data.
- Research Using Health Information from Deceased Individuals: This activity is limited to analyzing data (identifiable or not) about deceased individuals and the activities are not subject to the jurisdiction of the FDA. Note that deceased individuals cannot be Human Subjects according to DHHS, but may be subject to FDA jurisdiction, requiring IRB review

If you remain unsure about whether your project qualifies as human research or you desire documentation of the determination, you can submit the “[Human Research Determination Form \(HRP-503\)](#)” in ETHOS. Follow the directions for submitting a new study and upload the Determination Form under Question 9 on the first page of

web-based application in ETHOS known as the SmartForm. If you submit the Determination Form and it is determined that the project is human research, you will be asked to withdraw/discard and submit a new study with a fully developed protocol.

IMPORTANT: Determination forms must be submitted prior to the conduct of research. The IRB does not issue retrospective determinations, exemptions or approval of research already conducted.

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Can the IRB issue retrospective approval of research I have already conducted?

No, the IRB will not review determination forms or research protocols if the research has already been conducted. When applicable, IRB review provides guidance to the investigator and assurance to the public that ethical considerations and risks related to the research have been considered, mitigated when possible, and determined to be appropriate.

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What are the consequences of conducting human subjects research without prior IRB approval?

The consequences of conducting human subjects research without prior IRB approval are significant and could include some or all of the following:

- Required destruction of any data collected without IRB approval
- Journals may not publish or you may be prohibited from presenting research findings
- Retraction of any published research findings
- Loss or clawback of funding
- Other academic disciplinary actions initiated by your department, college or the University strongly encourages seeking a determination

If you are concerned that research you have conducted may have required IRB review, please email the IRB at irb@umn.edu to discuss.

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What data or specimen activities require IRB review and approval?

Depending on the nature of the activities, IRB review and approval may or may not be required. There are some activities that involve data and/or specimens that do not meet the definition of Human Research (see “[SOP: Definitions \(HRP-001\)](#)”) and therefore do not require IRB review and approval. It is important to know that even if IRB approval isn’t required, researchers are required to follow any other applicable requirements, policies, and procedures. This can include adherence to HIPAA. [Appendix B-2](#) describes IRB and HIPAA applicability and considerations regarding data or specimen related activities.

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Can an investigator de-identify data or specimens under his or her own control for future research use without IRB review and approval?

No. The investigator must submit each discrete research project for IRB review. New uses of data/specimens obtained for primary research purposes by an investigator with IRB approval (or exemption) require IRB review of an amendment or a new protocol describing the proposed secondary use, depending on the previous approval (or exemption) and the new research objective(s). Informed consent (or a waiver of informed consent) may also be required for this new use depending on the scope of the original consent and the newly proposed research.

See [Appendix B-2](#) which describes IRB and HIPAA applicability and considerations regarding data or specimen related activities. See also “[Is Consent required for secondary use research?](#)”

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Is consent required for secondary use research?

Research using previously collected data and/or specimens must be consistent with the scope and terms described in the original informed consent process/documents, as applicable. If consent was not obtained or the original consent does not adequately include the proposed secondary use, specific informed consent for the new research may be required. De-identification or coding of data/specimens should not be used as a means for circumventing the original terms of consent. Except in unusual circumstances, informed consent is required when identifiable data and/or specimens are used.

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Can an investigator share identifiable data or specimens with collaborators?

Investigators may not share identifiable data and/or specimens with collaborators (internal or external to the University of Minnesota) for secondary research purposes without IRB approval. In addition, transfers outside of the University of Minnesota require a material transfer agreement. (See [Data Transfer policy](#)).

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How does quality improvement differ from research?

Both research and quality improvement are systematic investigations that may involve human participants but they differ in important ways. A [Hastings Center workgroup](#) defines QI as systematic, data-guided activities designed to bring about immediate improvements in health delivery in particular settings. QI is an integral part of good clinical practice and is designed to bring about immediate improvements, human subjects research aims to generate new, generalizable, and enduring knowledge about human health ([Lynn et al., 2007](#)).

IRB approval may be required when the activity involves some of the following characteristics:

- seeks to develop new knowledge or validate new treatments rather than to assess the implementation of existing knowledge;
- when the methodology employs a standard research design, such as randomization;
- when the protocol is fixed with a rigid goal, methodology, population, time period, etc.;
- when the funding for the activity comes from the outside organizations such as the NIH or those with a commercial interest in the results;
- when there will be a delay in the implementation of results;
- when the risks from the intervention to participants are greater than minimal; or
- when the program being implemented for a research purpose or altered or controlled in some way to answer a research question.

In addition, a quality improvement project may constitute research if it involves introducing an untested clinical intervention for purposes which include not only improving the quality of care but also collecting information about patient outcomes for the purpose of establishing scientific evidence to determine how well the intervention achieves its intended results.

Determining whether a project constitutes research or Quality Improvement (QI) can be challenging. The IRB does not have the authority to retrospectively review or provide retroactive approval. Therefore, it is important to determine whether an activity meets the criteria for human subjects research or a QI initiative before the activity is initiated. Complete and submit the [Determination Form \(HRP-503\)](#) in ETHOS for an IRB determination.

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Does a quality improvement registry or database require IRB approval?

Generally no. A registry that is developed for the sole purpose of collecting information in the course of patient clinical care and is only used to measure the performance or quality of operations does not constitute human subjects research and does not require IRB review and approval.

If the QA/QI registry's purpose is to produce new knowledge regarding the relationship between specific procedures and health outcomes, IRB review and approval is required as the registry activities may constitute human subjects research.

If researchers request information from the registry for research purposes, IRB review and approval may be required. See "[What if I'm not sure my project requires IRB review?](#)"

Regardless of whether IRB approval is required for the registry, investigators are responsible for complying with all other policies and laws that pertain to the collection, storage, sharing, and use of information located in the registry.

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How do I submit new Human Research to the IRB?

Studies that meet the federal definition of human research require IRB approval before recruitment or other study-related activities can begin.

Create a New Study in ETHOS by clicking on the web-based application in ETHOS known as the SmartForm, attach all requested supplemental documents and submit the form by clicking the "Submit" activity. Before submitting the research for initial review, you must:

- Obtain the financial interest status ("yes" or "no") of each research staff; and
- Obtain the agreement of all study personnel to their respective roles in the research.
- Obtain the FDA Form 1572 (for FDA-regulated studies). Although you are not required to submit this, the IRB may request it during its review.

For complete submission instructions, see the [ETHOS job aids](#) including the [New Submission Checklist](#).

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Who is considered Study Personnel for purposes of IRB submission?

The following information provides guidance for adding research personnel to ETHOS. This guidance applies to both new applications and updates to existing, approved applications. Note that changes in personnel must be submitted to the IRB as they occur and activities associated with addition of these personnel must align with the original IRB approved aims and goals of the specific study.

For purposes of applying to the IRB, research personnel are individuals who:

- a. Interact with human subjects (e.g., informed consent process, manipulating subject's environment for research purposes, conduct invasive or non-invasive research procedures), or
- b. Are involved with collecting, reporting, or analyzing identifiable subject data, or
- c. Function outside of regular work practice to conduct research (e.g., student administering research testing),* or
- d. Are faculty advisors providing direct oversight of research involving human subjects, or human subjects' private information, or

e. Are listed on FDA Form 1572 (Statement of Investigator) even if (a) – (d) do not otherwise apply.

* If an individual is functioning within his or her regular work practice (e.g., performing his/her job providing clinical care as a physician but referring potential participants to a research study; a phlebotomist following standard practice collecting blood for research tests; or an x-ray technician following standard practice performing an x-ray for research , etc.) **and involvement in the research is limited to only those work responsibilities without further contribution to the research**, then such individuals do not need to be listed in ETHOS.

Funding agencies may have their own definition of research personnel (i.e., “key personnel”); however, researchers are required to comply with IRB guidance when listing personnel in ETHOS.

Individuals with the following roles must be included in the ETHOS study record:

1. Principal Investigator – the person responsible for the conduct of the study including leading the study team, when applicable;
2. Advisor of Student-Investigator – the person responsible for direct oversight of the study including leading the student-investigator;
3. Sub-Investigator(s) (or co-investigators) – any individual member of the study team who will perform study procedures and make research protocol decisions;
4. Study Coordinator;
5. Any other member of the study team to whom the investigator delegates responsibility for making research protocol decisions, including staff obtaining consent for research participation;
6. Staff collecting, reporting or analyzing identifiable subject data; and
7. Staff who will have subject contact and/or access to identifiable subject data.

Document study team members that are appointed as temporary/casual workers or volunteers at the University of Minnesota who do not have access to ETHOS by completing the ETHOS “[External Team Member Information Form \(HRP-216\)](#)” and selecting the appropriate section for “Volunteer” or “Temp/Casual.”

Please note that the Principal Investigator is responsible for ensuring all University and/or Department requirements regarding volunteers are met, including a signed University of Minnesota Volunteer Agreement (available in the [Contracts Library](#)). The completed contract is not required for IRB review. However, failure to keep documentation of the volunteer agreement as part of your research record is considered non-compliance with institutional requirements.

In “[External Team Member Information Form \(HRP-216\)](#)” also document external study personnel engaged in human research activities **ONLY IF** the University of Minnesota has agreed to serve as the IRB of record for that external institution or external collaborator under a Reliance Agreement or Individual Investigator Agreement (“IIA”).

Research staff listed on UMN human research studies must adhere to all laws, regulations, standards and requirements that govern research studies and clinical trials.

Documentation of completed human research protections training is required for all listed study personnel as part of the ETHOS submission. If training does not appropriately display in the Training tab of the STUDY submission in ETHOS (i.e. external personnel), you may be required to upload the certificate(s). See [required training](#) for more information.

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What are the expectations for UMP employees listed as study personnel?

UMP employees, other than physicians, without University appointments can be asked by University PIs to assist on human research studies. To do so, UMP staff must be listed on the IRB application in ETHOS. UMP employees without active UMN internet IDs must request a guest account to be listed on an ETHOS IRB submission. A link to request these accounts can be found on the [ETHOS log-in webpage](#).

Research staff listed on UMN human research studies must adhere to all laws, regulations, standards and requirements that govern research studies and clinical trials.

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What is the distinction between social behavioral research and biomedical research?

Biomedical research

Biomedical research refers to the study of specific diseases and conditions (mental or physical), including detection, cause, prophylaxis, treatment and rehabilitation of persons; the design of methods, drugs and devices used to diagnose, support and maintain the individual during and after treatment for specific diseases or conditions; and/or the scientific investigation required to understand the underlying life processes which affect disease and human well-being, including such areas as cellular and molecular bases of diseases, genetics, immunology. This research is typically quantitative and not qualitative. Biomedical research is often patient-oriented and the research involves:

- Studies of mechanisms of human disease
- Studies of therapies or interventions for disease
- Clinical trials (see “[SOP-Definitions \(HRP-001\)](#)”)
- Studies to develop new technology related to disease

Social-Behavioral Research

Social-behavioral research refers broadly to research that deals with human attitudes, beliefs, and behavior and is often characterized by data collection methods such as questionnaires, interviews, focus groups, direct or participant observation, and non-invasive physical measurements. It may include physical outcomes as they relate to psychosocial processes which may increase the risk of poor health outcomes, but excludes the study of patient populations identified by their diseases/disorders or studies of the mechanisms of specific human diseases. The research may be qualitative or quantitative. Social-behavioral research also includes epidemiological or outcomes research and health services research:

2. **Educational studies:** These types of studies examine the effectiveness of educational programs, practices, and policies, including the application of technology to instruction and assessment.
3. **Epidemiological and behavioral studies:** These types of studies examine the distribution of disease, the factors that affect health, and how people make health-related decisions.
4. **Outcomes and health services research:** These studies seek to identify the most effective and most efficient interventions, treatments, and services.

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When is social behavioral research subject to biomedical research requirements (i.e., regulatory, training, etc.)?

Social-behavioral studies that involve the use of drugs or devices, radiation and radiolabeled tracers, and other invasive procedures require review by a biomedical IRB panel and subject to any additional regulatory

requirements as appropriate. In addition, the principal investigator and study personnel must complete the biomedical training requirements (see “[Human Research Education and Training \(HRP-066\)](#)”).

Prospective collection of biological specimens (e.g., blood, saliva) and/or collection of data via non-invasive measures (e.g. magnetic resonance imaging without the use of radiotracers, tests of sensory acuity, electrocardiography) that are usually considered clinical in nature may be reviewed by a social-behavioral IRB panel if:

1. The purpose of the research is primarily social-behavioral in nature; and
2. The physiological interventions are sufficiently benign as to involve no more than minimal risk to subjects.

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How do I write an Investigator Protocol?

For all new studies submitted for IRB review in ETHOS, investigators will complete a brief smart-form, provide a research protocol and attach any relevant study materials (e.g., recruitment material, consent forms, instruments, brochures). Only [IRB approved templates](#), or departmental templates pre-approved by the HRPP, may be used. Available template protocols include:

1. “MEDICAL TEMPLATE PROTOCOL (HRP-590)”
2. “SOCIAL TEMPLATE PROTOCOL (HRP-580)”
3. “DATA & SPECIMEN TEMPLATE PROTOCOL (HRP-595)”
4. “HUD TEMPLATE PROTOCOL (HRP-596)”
5. “DATABASE/REGISTRY/REPOSITORY TEMPLATE PROTOCOL (HRP-597)”

Use the applicable template protocol as a starting point for drafting a new Investigator Protocol and reference the instructions in italic text for the information the IRB looks for when reviewing research. Here are some key points to remember when developing an Investigator Protocol:

- There are two versions of each protocol template, one with italicized instructions and one without. Use the version with italicized instructions as a reference when completing the version without instructions;
- The protocol should not be too broad of purpose. A grant is not a protocol and will not be accepted as an IRB submission. Aims should not be copied verbatim from a grant submission. If there are multiple aims that will be addressed in multiple sub-projects, each should be submitted separately with a protocol.
- If you received a sponsor’s protocol, use “LOCAL PROTOCOL ADDENDUM (HRP-508)” instead to describe your local activities;
- Only upload a WORD version of the protocol in ETHOS. PDFs are generally not accepted.
 - If a sponsor provides a PDF version of the protocol, request a WORD version of the protocol from the sponsor.
 - The IRB recognizes that not all sponsors will provide a WORD version of a protocol due to document ownership and version control concerns. If this happens, the investigator should submit the PDF version of the protocol and ‘Add a Comment’ to the submission indicating that the sponsor will not provide a WORD version for IRB review.
 - In the event of changes to a sponsor protocol (in PDF format), when submitting to the IRB the revised protocol PDF, the revision should note in detail the summary of changes. This summary

should be appended to the protocol PDF file using the 'Import Page/File' or 'Add Page/File' feature of Adobe. The summary should be inserted at the beginning of the protocol PDF.

- Note that, depending on the nature of your research, certain sections of the template may not be applicable to your Investigator Protocol. Indicate "N/A" as appropriate, but do not delete those sections;
- Other study related materials should not be appended to the study protocol. Instruments, tests, surveys, and recruitment material should be uploaded separately in ETHOS for IRB review.
- You may not involve any individuals who are members of the following populations as participants in your research unless you indicate this in your inclusion criteria as the inclusion of participants from these populations has regulatory implications:
 - Children;
 - Pregnant women;
 - Prisoners;
 - Adults lacking capacity to consent and/or adults with diminished capacity to consent;
 - Non-English speakers;
 - Those unable to read (illiterate);
 - Employees of the researcher; and/or
 - Students of the researcher.

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How do I create recruitment material?

Recruitment is the initial step of the informed consent process. There are two strategies to recruitment, passive and active. Passive recruitment involves the distribution of recruitment material and active recruitment occurs when research staff approach and interact with specific individuals with an aim of enrolling them in research (Gelinas et al. 2017).

Whether passive or active, the recruitment plan should be described in the protocol and the recruitment materials must be provided to the IRB in the ETHOS submission. When developing a recruitment plan, investigators should comply with any local, state, or federal requirements.

Investigators should adhere to any organizational or institutional requirements. Review University guidelines and requirements when considering the use of social media related recruitment strategies. If the recruitment plan involves the use of Fairview patients, staff, or resources, review [Fairview Research Administrations requirements](#).

Recruitment materials can include:

- Recruitment letters
- Scripts for telephone or in-person discussion
- Flyers, posters, postcards, newspaper ads, press releases intended for recruitment with study team contact information
- TV and/or radio spots
- Websites/internet ads Electronic mailings (e.g., email, text)
- Social media pages, ads, blogs, tweets, etc.

In addition, if you plan to include video-based recruitment materials, provide a script and screen shots. See [WORKSHEET: Advertisements \(HRP-315\)](#) for guidance on what must or must not be included in recruitment material.

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How do I develop a compensation plan for research participation?

Researchers may choose to offer payment to research participants for a variety of reasons. Payment is sometimes offered to compensate participants for their time and assumption of research-related burdens or for services provided, such as reimbursing participants for out-of-pocket expenses related to participation. The IRB does not have a policy that indicates how much or how little research participants should be compensated for research participation. Participants should be paid in proportion to their time and inconvenience as a result of participation in the research study. Compensation is not considered a benefit.

Researchers must ensure that offers of payment never compromise understanding of a research study or otherwise distort an individual's decision to participate in research, thus undermining or even invalidating informed consent. The amount of payment and the proposed method and timing of disbursement is neither coercive nor presents undue influence.

Online crowdsourcing platforms such as Amazon MTurk pose issues that may not exist in more traditional research recruitment settings. Amazon MTurk describes itself as a crowdsourcing marketplace that makes it easier for individuals and businesses to outsource their processes and jobs to a distributed workforce. Given the non-research-oriented nature of the website, investigators planning to use MTurk for recruitment purposes are expected to outline an equivalent hourly rate for participants in the study. If offering less than an hourly rate per the current definition of a living wage for Hennepin County (see <https://livingwage.mit.edu/counties/27053>), the investigator must provide a justification for doing so in the protocol for the IRB to review.

There are online recruitment platforms such as Lucid, Time-sharing Experiments for the Social Sciences (TESS) and Prolific that are focused on finding participants for research. Some of these platforms have a pre-established compensation structure that a principal investigator may have limited or no influence over. If using such a platform, please explain that platform's compensation structure.

When using an online recruitment platform the consent form must include details on any additional privacy and confidentiality guidelines you will follow. For example, ensure participants that you won't collect their platform ID. If you need to have the ID, ensure that it will be kept confidential and secure, not linked back to the survey data, and deleted after use. This information must be included in the consent document and in the confidentiality of the IRB protocol.

See [WORKSHEET: Payments \(HRP-316\)](#) for additional guidance.

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How do I create a consent document?

Use the consent template most appropriate for your study. All consent templates are available in the [HRPP Toolkit Library](#).

When a consent template is developed by a sponsor or the study will rely on an external IRB, ensure that the consent template includes the University's required language noted in "[WORKSHEET: Local Context Review for Relying on an External IRB \(HRP-830\)](#)."

Note that all long form consent documents and all summaries for short form consent documents must contain all of the required and all additional appropriate elements of consent disclosure. Review the “Long Form of Consent Documentation” section in the IRB’s [“WORKSHEET: Criteria for Approval \(HRP-314\)”](#) to ensure that these elements are addressed. The templates have been revised to address new elements of consent in the revised Common Rule, including the requirement to begin the consent process with a presentation of key information. These templates can be used before the revised Common Rule is in effect as the documents do not conflict with the pre-2018 Common Rule.

For specific requirements for both the informed consent process and the documentation of participants’ consent to participate in research, see also [“SOP: Informed Consent Process for Research \(HRP-090\)”](#) and [“SOP: Written Documentation of Consent \(HRP-091\).”](#)

The IRB strongly encourages investigators to utilize ETHOS during the consent process, by downloading the current IRB approved consent form(s) during enrollment of new participants. Utilizing ETHOS records for this process will minimize investigator errors associated with use of an incorrect consent form version.

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How do I create an assent document?

Use the [“TEMPLATE ASSENT DOCUMENT \(HRP-583\)”](#) to create an assent document or [“TEMPLATE ASSENT SCRIPT \(HRP-584\)”](#) to create an assent script.

There is no specific age for when assent is required. You are expected to create an assent form that is age-appropriate and study-specific, taking into account the typical child's experience and level of understanding, and composing a document that treats the child respectfully and conveys the essential information about the study. The IRB will ultimately make a determination as to whether assent is required on a study-by-study basis.

The document should be child friendly in content and appearance. Illustrations might be helpful, and larger type makes a form easier for younger children to read. Studies involving older children or adolescents should include more information and may use more complex language. Parental consent forms also may be revised to include the assent of older children, provided the directive language is revised and the appropriate signature and date lines are added.

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How do I create an information sheet?

In circumstances where the research involves an option for a child whose illness has not responded to other available treatments or for whom standard therapies are not suitable, it is unlikely that a child’s refusal to participate would be honored. In such cases, it is more appropriate to provide children with an information sheet that contains the same information as an assent form would, but without the indication of choice. This respects the child’s right to understand the research and what will happen to him/her, while acknowledging that there are situations in which a parent’s authority must override the wishes of the child.

Additional information about the inclusion of children in research is included in [“CHECKLIST: Children \(HRP-416\)”](#).

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How do I create a parental permission document?

For research involving children, generally one or both parents give permission on behalf of a child to participate in research. Use the [“TEMPLATE PARENTAL PERMISSION DOCUMENT \(HRP-585\)”](#) to create a permission document. Depending on how your research is approved, one or both parent signatures may be

required. Consult “[CHECKLIST: Children \(HRP-416\)](#)” to evaluate the criteria the IRB uses to determine the level of risk and required signatures for your research to decide how many signature blocks you should include on your parent permission document.

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Can I conduct consent by telephone or by mail?

Remote consent by phone may be considered on a case-by-case basis and should be appropriate for the study. Consent discussions may take place by phone in situations where it is not possible for the participant/legally authorized representative (surrogate) to meet with the investigator in person. When investigators anticipate the need to obtain informed consent by phone, they should justify in the protocol submission why this is necessary and describe how the phone consent process will be operationalized and documented. The remote (phone) consent process must be approved by the IRB.

Remote consent by mail may also be considered for certain minimal or low risk studies where some or all of the potential subjects are unable to meet with the investigator in person due to logistical or other reasons. When investigators anticipate the need to obtain informed consent by mail, they should justify in the protocol submission why this is necessary and describe how the mail consent process will be operationalized and documented. The remote (mail) consent process must be approved by the IRB.

When documentation of informed consent is required in writing, the consent form is sent to the prospective subject by USPS or other mail carrier, or electronically. If the consent form is sent and returned by mail, include two copies - one for the subject to keep for their records. The person reads the consent form and contacts the investigator if s/he wishes to discuss participation in the study or has any questions about the study. If the person agrees to be in the study, they sign and date the consent form and return it by mail, or electronically to the investigator. When there is a line for signature of the person obtaining informed consent in the consent form, the person verifying informed consent would sign and date the consent form upon receipt.

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Can I conduct consent electronically?

Whether part or all of the eIC process takes place on-site or remotely, the responsibility for obtaining informed consent remains with the investigator and the study personnel to which responsibility has been appropriately delegated. The investigator cannot delegate authority to obtain informed consent to the electronic system. Digital signatures must also meet state law requirements.

Electronic informed consent (eIC) may be used to either supplement or replace paper-based informed consent processes in order to best address the participant’s needs throughout the course of the study. For example, some participants may prefer one method over another. Other participants may have difficulty navigating or using electronic systems because of, for example, a lack of familiarity with electronic systems, poor eyesight, or impaired motor skills. In such cases, the eIC process may not be appropriate for these participants. Therefore, participants should have the option to use paper-based or electronic informed consent methods completely or partially throughout the informed consent process.

Investigators must provide a detailed e-consent plan within the protocol for IRB review. The investigator should submit copies of the consent form (WORD version only) at the time of IRB submission and review. **Do not** develop the consent form in the eIC platform until the consent form receives IRB approval. After developing the eConsent document, investigators should provide a link or screen capture document via a Modification submission to the IRB. The IRB will confirm whether the electronic version is in compliance with the IRB approved Word version.

In addition, the investigator should submit any informational materials, including any videos or web-based presentations, which the participant will receive and view during the eIC process. For more guidance on developing an e-consent plan see [Use of Electronic Informed Consent Questions and Answers: Guidance for Institutional Review Boards, Investigators, and Sponsors](#).

Investigators must obtain IRB approval prior to implementing any changes to the informed consent form, whether electronic or hard copy. See [“How to submit a Modification?”](#)

Moreover, in some circumstances, it may be appropriate for investigators or study personnel to assist participants in using the eIC technology. For example, study personnel may help the subject navigate the consent by clicking on links for the participant ([FDA – OHRP Guidance on Electronic Consent](#)).

For FDA regulated research or research data that will be submitted to the FDA in the future as part of a marketing application or other FDA related application, the electronic consent process and platform must meet the [requirements of 21 CFR part 11](#). Failure to comply with 21 CFR part 11 will result in noncompliance and the FDA may determine that the information collected cannot be used. The University of Minnesota’s REDCap e-Consent module is Part 11 compliant.

See [WORKSHEET: Criteria for Approval \(HRP-314\)](#), [SOP: Informed Consent Process for Research \(HRP-090\)](#), and [SOP: Written Documentation of Consent \(HRP-091\)](#) for more information.

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How do I obtain signatures electronically?

"Digital signatures" may be acceptable forms of documentation of written informed consent. Electronic, computer or tablet-based consent documents may facilitate record keeping even when an individual is present and could sign a paper form. Digital signatures may be considered for face-to-face and remote consent, but the technologies and processes used must be described in the protocol.

There are two forms of digital signatures: (1) actual signatures on tablets or computers (where an individual uses a stylus or finger to make a representation of their signature, as available in many retail stores) OR (2) validated electronic signatures on platforms with password entry (such as those used to sign medical notes or electronically write prescriptions). Validated electronic signatures typically require one to "set up" an identity and password within an electronic system and may not be easily and rapidly activated. Both forms of digital signature may be used in research in certain settings, but because of tracking, privacy and identity validation issues, this may be more challenging than it initially appears.

Both 'digital signature' methodologies, if used entirely remotely, are generally approved only for low-risk research or other circumstances (i.e., time of national emergencies, pandemics, natural disasters) because it is not always possible to validate the identity of the individual "on the other end of the computer." When a stylus is used to collect a signature in person, the usual methods of identity validation should be used (typically a patient is asked to provide a picture identification card when they check in at the clinic).

Note: Scanned signatures that are copied and pasted to a document are not acceptable "digital" signatures.

For FDA regulated research, the digital signature platform and process must be [21 CFR part 11 compliant](#). In addition, the research team must verify the participant’s identity. If the entire consent process takes place at the

study site, the study personnel can personally verify the participant's identification, review the eIC content, answer questions about the material, have follow-up discussions, and witness the signing of the eIC.

See [WORKSHEET: Criteria for Approval \(HRP-314\)](#), [SOP: Informed Consent Process for Research \(HRP-090\)](#), and [SOP: Written Documentation of Consent \(HRP-091\)](#) for more information.

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How do I protect the security and confidentiality of research data?

You are expected to plan for the appropriate protection of data that could be identified with individuals or groups through mechanisms appropriate to the medium in which the data are collected, analyzed, stored, or transmitted. You must document this plan in your protocol and explain the provisions for confidentiality to prospective participants during the consent process and within consent documents.

If appropriate, a waiver or alteration of the consent process or waiver of written documentation of consent may be requested in order to provide an additional measure of confidentiality.

Additional information and required language can be found in the “[Social-Behavioral Consent Template \(HRP-582\)](#),” “[Biomedical Consent Template \(HRP-592\)](#),” “[CHECKLIST: Waiver or Alteration of Consent Process \(HRP-410\)](#),” and “[CHECKLIST: Waiver of Written Documentation of Consent \(HRP-411\)](#)” and in the [protocol templates](#).

In order to manage data security risks, units and University community members must ensure that their electronic devices and other resources which store, transmit, or process University information meet the information security processes and standards contained in the [Information Security Policy](#).

For most types of Human Subject research University policy requires that a professional IT organization manage the systems or that an exception to University policy is filed. If you [manage your own research data](#) storage or IT systems, a [gap analysis](#) to the University information security standards is required. This may also be useful for a Data Management Plan. The following are additional resources that may be helpful:

Policies

- [Policy and Guidance for Information Security](#)

Guidance

- [Classifying Research Data](#)
- [Practices for the Information Security policy](#)

Procedures

- [Setup and Use Two Factor Authentication](#)
- [Enable Security Features on your Device](#)
- [Administrative Privileges: What you need to know.](#)

For more information, see [Know Your Data and How to Protect University Data](#), or contact your local IT support or [Technology Help](#). Consult [University Information Security](#) when you have questions involving private data, the security of technology provided by a vendor. UIS staff also consult with University members on information security in architecture, software acquisition, governance and compliance requirements, business processes, and network design. Email: security@umn.edu.

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Can I store source / study documents electronically?

Generally, yes. However, if you plan to store study related documents, including source documents electronically, you or your department should develop a standard operating procedure on how documents will be scanned, certified, and stored electronically. Industry and other Sponsors generally have specific requirements for electronic records to comply with 21 CFR Part 11, when applicable. Investigators should seek the written permission of the Sponsor and follow the Sponsor's requirements for electronic storage of source documents prior to creation of electronic source document storage. Documentation of Sponsor permission should be filed with study documents.

Source documents/consent forms should be scanned individually and labeled. The person who certifies the copy as an accurate and complete representation of the original, having all the same attributes and information as the original, should be the same person who actually created the electronic copy from the original. Different software and applications can be used to create certified copies. For FDA regulated research documentation, systems and processes should be FDA compliant (including 21 CFR Part 11). In addition, systems must comply with University of Minnesota policies and procedures for research data storage (see [“How do I protect the security and confidentiality of research data?”](#)).

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How do I protect the privacy of research participants when using Zoom or other video conferencing tools?

An increasing number of video data collection studies now involve investigators recording a participant in their home via Zoom or another platform (e.g., video recording an interview so that the PI can evaluate the body language of the interviewee). There are a number of considerations about confidentiality of the participant and others in their environment in these situations. Investigators should review the guidance made available by the Health Information Privacy and Compliance Office when developing study activities that will involve video or other media collection procedures.

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Does the General Data Protection Regulation (GDPR) affect my research?

The GDPR regulates collection, storage, and processing of any personal data collected from individuals present in the EU at the time the information is collected. Research or other sponsored activities involving the collection of such regulated personal data, including clinical trials with participants in the EU, would thus be affected. The allocation of responsibility for GDPR compliance should be agreed to explicitly with EU collaborators, EU sub-recipients and any third party used for processing of data (including storage and analysis of the data) whether the processor is located in the EU or not. Consent form content, personal data handling, and reporting (in the event of a breach of confidentiality) are all research and trial areas governed by the GDPR. See [Appendix A-9](#) and [University of Minnesota's GDPR Information Statement](#) for more information.

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What is a COC (Certificate of Confidentiality)?

A Certificate of Confidentiality (COC) protects the privacy of research participants by prohibiting forced disclosure of their individually identifiable, sensitive research information to anyone not associated with the research, except when the participant consents to such disclosures or in other limited specific situations.

Effective October 1, 2017, all ongoing or new research as of December 13, 2016 that is:

- funded wholly or in part by the NIH and
- collects or uses identifiable, sensitive information

will be automatically issued a Certificate of Confidentiality as a term and condition of the NIH grant award. Certificates will no longer be issued in a separate document. The Notice of Award and the NIH Grants Policy Statement will serve as documentation of the Certificate protection.

NOTE: The intent of a COC is to prevent forced disclosure of identifiable participant information (for example, in response to a subpoena or other legal demand). The intent of a COC is not to withhold this information from individuals at the research institution who need access in order to perform their job duties (for example, information needed for scheduling a participant for a study visit).

NIH-funded research conducted internationally and meets NIH's criteria for a COC will still be considered to have been issued a COC, however the enforceability of the COC is uncertain in foreign jurisdictions.

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What are my responsibilities for a Certificate of Confidentiality?

Researchers are required to determine whether their research records generated with NIH funding are covered by a COC.

Determine applicability of the NIH COC Policy:

1. Was the research begun or ongoing on or after December 13, 2016?

If the answer is “no”, the policy does not apply. If the answer is “yes”, answer the following questions.

2. Is the research conducted or funded wholly or in part by NIH?
3. Is the activity biomedical, behavioral, clinical, or other research?

If the answer to either question 2 or 3 is “no”, then the activity is not issued a CoC and the policy does not apply. If the answer to both is “yes”, answer the following questions:

4. Does the research involve human subjects as defined by 45 CFR Part 46?
5. Are you collecting or using biospecimens that are identifiable to an individual as part of the research?

The term “identifiable, sensitive information” means information about an individual that is gathered or used during the course of biomedical, behavioral, clinical or other research where the following may occur:

- a. An individual is identified; or
 - b. For which there is at least a very a small risk that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.
6. If collecting or using biospecimens as part of the research, is there a small risk that some combination of the biospecimens, a request for the biospecimens, and other available data sources could be used to deduce the identity of an individual?
 7. Does the research involve the generation of individual level human genomic data?

If the answer to any of the questions numbered 4-7 is “yes”, then a CoC is automatically issued and the policy applies.

8. If the policy applies, submit a Modification or a Modification/Continuing Review in ETHOS and review responsibilities to communicate to subjects.

Communicate COC coverage to study subjects:

- Is the research still open to enrollment?

When a COC covers the research records, and informed consent will be obtained from participants, the participants must be told about the protections afforded by the COC and any exceptions to those protections. Consent form templates have been revised to include language² that addresses the COC policy. This language must be present in consent forms of studies to which the policy applies so that all subjects signing a consent form receive the information. Subjects who have already signed a consent form do not need to sign another (re-consent) solely for this purpose, but researchers may choose to re-consent subjects if this approach works best for them. Submit revised consent forms to the IRB for review. See below for more details.

See [“Consent Form Template for Medical Research \(HRP-592\)”](#) or [“Consent Form Template for Social/Behavioral Research \(HRP-582\)”](#) for COC template language.

- What about subjects who have already signed a consent form for the study?

When a COC covers the research records for studies and informed consent has already been obtained from participants, researchers can prepare an information sheet that speaks to the protections afforded by the COC and the exceptions to those protections. All participants in the study should be sent or given a copy of the information sheet and a note made in the study record that the information sheet has been provided. A template information sheet for COCs is in the toolkit library under “Templates”. Submit revised consent forms to the IRB for review.

Researchers must be aware that information protected by a COC and all copies are subject to the protections of the COC in perpetuity. If a secondary researcher receives information protected by a COC, the secondary researcher is required to uphold the protections. Researchers who provide a secondary researcher with data protected by a COC should inform the secondary researcher of the continuing obligation to protect the data.

Researchers should also be aware that if the study continues to enroll additional participants after your NIH funding ends, those participants will not be protected by the Certificate unless you apply for a Certificate following the process for non-federally funded research.

Researchers should also be aware that certificates will be issued for applicable research regardless of the country where the investigator or the protected information resides though a COC may not be effective for data held in foreign countries.

Should you ever receive a subpoena, or any other legal process request seeking disclosure of research records do not release any records or information before you have contacted the:

- University of Minnesota Office of the Vice President for Research (OVPR) <https://research.umn.edu/> and the Office of the General Counsel (OGC) <https://ogc.umn.edu/>.
- The OGC will assist researchers with responding to the legal request for records, and with enforcing the privacy protections.

For complete information about the policy, including FAQs, go to:
<https://humansubjects.nih.gov/coc/index>.

Certificates of Confidentiality for 1) Other HHS agencies (Non-NIH), 2) Non-HHS Federal Funders, or 3) Non-Federal Funders

A number of other HHS agencies also issue CoCs. For information and instructions go to: <https://humansubjects.nih.gov/coc/index>.

Information and templates for requesting a CoC when the funding source is not an HHS agency, or when the funding source is not federal can also be found at the link above.

Non-Federally funded researchers who are applying for a CoC need to use the Online Certificate of Confidentiality System to request a Certificate of Confidentiality (CoC), issued by NIH.

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What are my responsibilities for data security?

If your protocol proposes use of any non-standard technology for data collection and management, you should provide documentation demonstrating that the technology is appropriately secure. In addition, you are expected to follow all University data security policies and procedures when conducting research.

In the case of research involving sensitive data, the IRB will require you to include a robust security plan in your protocol and verify compliance with the University's [Data Security Policies](#). Additional policies that apply include the University's [Data Security Classification](#) and [Information Security](#) policies.

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What about HIPAA?

The [Health Information Privacy and Compliance Office](#) is responsible for ensuring that all University research complies with the Health Insurance Portability and Accountability Act (HIPAA). Questions regarding HIPAA compliance should be directed to that office.

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Does my research require scientific assessment?

The purpose of scientific assessment is to encourage the development of scientifically sound medical research. To justify the inclusion of human participants in research, and to assess the balance between any risks that may be imposed upon participants with the utility of the outcomes of the investigation, an assessment is required to evaluate the scientific question and appropriateness of the methods planned to answer the scientific question. This assessment establishes an initial foundation that allows further assessment; IRB reviewers know as they initiate assessment that the study is powered to yield results.

The review must be performed by independent reviewers; therefore, members of the research team cannot participate in this review. Only one method of scientific review (see below) is required prior to review by the IRB.

Scientific assessment is required for medical research that is not exempt under CFR 45 §46.101 (b) or does not qualify for expedited review under CFR 45 §46.110. Research reviewed by the full committee IRB in order to determine whether it qualifies as a Non-Significant Risk (NSR) IDE study does not need documentation of scientific assessment prior to IRB review. However, if the IRB disagrees and finds the study to be Significant Risk (SR) IDE, scientific assessment must be obtained. Scientific assessment applies to the actual clinical research protocol which describes in detail the involvement of human participants.

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Acceptable Methods for Scientific Assessment

There are four possible mechanisms for scientific assessment:

1. Nationally-based, federal funding organizations (NIH, NSF) when research projects have been subjected to full peer review (e.g., review by a study section or grant committee);
 - The actual protocol being submitted to the IRB must have been reviewed in its current form. Peer review of a grant that describes a clinical trial in general terms does not satisfy this criterion.
 - Industry-sponsored clinical trials designed by the sponsor with or without external consultants **do not** satisfy this criterion for independent peer-review.
2. Nationally based non-federal funding organizations (March of Dimes, American Academy of Pediatrics) employing peer review mechanisms for awarding of funding;
 - The actual protocol being submitted to the IRB must have been reviewed in its current form. Peer review of a grant that describes a clinical trial in general terms does not satisfy this criterion.
 - Industry-sponsored clinical trials designed by the sponsor with or without external consultants do not satisfy this criterion for independent peer-review.
3. Locally constituted mechanisms using peer review for awarding of funding, or for permission to use resources, including:
 - Cancer Protocol Review Committee (CPRC)
4. All other applicable medical research not reviewed under one of the methods above:
 - HRPP facilitated scientific assessment is requested via ETHOS.
 - HRPP facilitated scientific assessment is requested via ETHOS. Download the [HRPP Scientific Assessment Submission Guide](#) for how to submit a request for HRPP scientific assessment. You must also complete [Scientific Review \(HRP-538\) located in the Templates section](#) of the Toolkit Library. [Gillette Children's Specialty Healthcare Scientific Review](#) is accepted for research conducted by Gillette affiliated PIs.
 - Review by a biostatistician is required for all applicable research prior to scientific assessment under this method.

In most circumstances, medical applications requiring full committee review will not be assigned to a meeting until documentation of scientific review is provided. Exceptions to this requirement include HUD protocols and expanded access protocols. If you have questions regarding the applicability of additional scientific assessment to your protocol, please contact the IRB office.

The IRB shares in the responsibility for scientific assessment and will further evaluate whether you have the resources necessary to protect participants as reviewers evaluate the criteria for approval.

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What happens during a HRPP facilitated scientific assessment?

HRPP scientific reviewers are asked to evaluate the research using “[Checklist: Scientific Assessment \(HRP-420\)](#).”

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What other reviews are required for my research?

In order to assure that all the criteria for approval have been met and that the necessary institutional or healthcare component approvals are in place, the IRB must rely on other components of the system-wide HRPP to review and approve their respective aspects of human research studies. Some ancillary approvals are required prior to IRB review; others are required prior to the IRB granting final approval.

HRPP staff, in consultation with IRB members, may also assess the need for involvement of other review committees or components of the HRPP on a case-by-case basis. You are responsible for meeting the requirements of all applicable reviewing components.

Information about the ancillary review process and the impact of various component reviews is included in the “[WORKSHEET: Ancillary Review Requirements \(HRP-309\)](#).”

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Do training grants or program grants that have cores require IRB review?

If a grant does not directly support human subject research, IRB review and approval is not needed unless required by the funding agency. Please contact the IRB Office for instructions on how to submit these for review if documentation of review is required.

NOTE: Any human subject research studies that receive funds from the grant to support the proposed research will require IRB review and approval.

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What if I'm receiving a grant award but my plans for Human Research are not fully defined?

Some applications for grants, cooperative agreements, or contracts are submitted to funding agencies with the knowledge that subjects may be involved within the period of support, but definite plans would not normally be set forth in the application or proposal. Often in these cases, grant money is sought to develop or refine plans for inclusion of human subjects at a future time.

These proposals may include projects where activities are yet to be identified or research staff need to be hired, or projects where instruments or plans need to be developed.

If you find yourself in this situation, the grant need not be reviewed by the IRB before an award may be made. Please contact the IRB Office for instructions on how to submit these for review if documentation of review is required.

NOTE: No human subjects may be involved in any project until the project has been fully reviewed and approved by the IRB.

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What if I applied for federal funding and received a Just-in-Time notification?

Just-in-Time (JIT) notifications from federal agencies advise investigators of the requirement to secure IRB review (among other requirements) prior to any distribution of funding. This requirement is time sensitive. The IRB will attempt to prioritize JIT requests to the best of its ability and provide timely and ongoing communication with researchers about the progress of the submission's review but investigators should be aware of and account for IRB review turnaround time when submitting.

For IRB submission of JIT requests, there are two submission paths available:

1. Complete IRB submission (with Protocol and all study-related materials): Use this path when all study documents (protocol, consent, etc.) have been developed and vetted through NIH at the time of JIT notice. For this instance, you would submit the following via a new study in ETHOS:

- a. All required IRB documents (protocol, consent, etc.)
- b. Documentation from the funding agency indicating JIT along with the timing requirement so that staff are aware of the time-sensitive nature of the submission.

The submission would then undergo pre-review and IRB review for a formal determination. Include the JIT related comment (see [Create and Submit a Just in Time Submission](#)).

2. Incomplete IRB submission (partially completed protocol/study materials): Only use this path if you cannot submit a completed IRB submission at the time of receiving a JIT notice. In the event you have not yet developed your full protocol, it may be acceptable to your funder to request a “Proof of Concept/Delayed Onset Human Research” determination. In this instance, you would submit the following via a new study in ETHOS:
 - a. [Human Research Determination Form \(HRP-503\)](#)
 - b. Documentation from the funding agency indicating JIT along with the timing requirement

This review is used to indicate that a federal grant or contract for human subjects research meets the federal regulatory criteria for allowing funds to be released. This type of determination does not constitute an exemption or IRB approval for research activities to begin. This is subject to the restriction that none of the funds may be used for human subjects research activities.

In order to conduct human subjects research activities after receiving a “Proof of Concept/Delayed Onset Human Research” determination, you must submit a New Study submission in ETHOS for full IRB review and approval. You cannot submit a Modification submission.

Please reference the “Create and Submit a Just in Time Submission” on the IRB website for additional guidance and instructions.

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Is there a fee for IRB review?

Review Fee for Business- and Industry-Sponsored Projects Reviewed by the University of Minnesota IRB

The IRB assesses a one-time \$2,500 fee for initial full IRB committee review of all greater than minimal risk business-and-industry sponsored clinical trials. All initial study submissions to the IRB must identify the funding sources supporting the proposed research. Fee eligible studies will not receive full IRB Approval until the billing information has been provided.

IRB applications that are dependent on state, federal, non-profit foundations or internal funds will be excluded from the IRB fee as those review costs are covered by indirect costs. Investigator-initiated studies are also excluded from the review fee.

Under extenuating circumstances, and with appropriate documentation to support such circumstances, you may request a fee waiver from the HRPP Executive Director. It is normally expected that you or contracts staff incorporate and negotiate the IRB review fee into the research contract.

Review Fee for Studies from Fairview or Gillette Investigators

The University IRB acts as the IRB for Fairview Health Systems and Gillette Children's Specialty Healthcare. Researchers whose sole affiliation is with Fairview Health Systems are assessed a fee for initial review of each study submitted. A negotiated fee is paid annually by Gillette Children's Specialty Healthcare.

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Human Research with Special Study Populations

What if I'm including a vulnerable population?

Vulnerable or potentially vulnerable populations are subject to additional protection under both federal regulations and IRB policy. Review the "[WORKSHEET: Vulnerable Populations \(HRP-333\)](#)", as well as the individual Toolkit documents specific to the population you are enrolling as referenced in your protocol template, to ensure you have provided sufficient information.

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What if I'm doing research involving prisoners?

Review "[CHECKLIST: Prisoners \(HRP-415\)](#)" to ensure that you have provided sufficient information in the research protocol.

Following IRB review and approval of DHHS-supported research involving prisoners, the IRB will provide a certification letter to the Office of Human Research Protections (OHRP) as required in 45CFR46.306.

When Subjects Become Prisoners during a Research Protocol

Once the research has commenced, similar considerations apply when a participant becomes a prisoner at any time during the conduct of the study, regardless of study funding. In this event:

- Report this to the IRB using the RNI Form in ETHOS; and
- Review "[CHECKLIST: Prisoners \(HRP-415\)](#)" to ensure you have provided sufficient information.

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What if I'm doing research involving children?

If your research involves children under the age of 18, review the "[CHECKLIST: Children \(HRP-416\)](#)," "[POLICY: Minnesota Laws Affecting Human Research \(HRP-112\)](#)" to ensure that you provide sufficient information in your protocol. Consider whether parental permission and assent should be obtained and incorporate this information in your protocol.

Consider how the research team will approach potential encounters with children in foster care and the implications for obtaining parental permission in these situations. Guardians of foster children may or may not have the right to consent for medical care for a foster child in their care. Foster parents' authority to make decisions on behalf of foster children varies significantly. Even though an agency may acquire legal authority to place a child through a voluntary placement agreement between the agency and the child's parent, this does not mean that the agency has the authority to make major life decisions regarding the child, including major medical decisions (<https://www.revisor.mn.gov/statutes/2011/cite/260D.02> (subd. 11)). Thus, a parent retains the authority to provide legal consent for their child in foster care unless the parent has been stripped of parental rights or has agreed to relinquish parental rights through a court proceeding. However, if parental rights have been stripped or voluntarily relinquished and the child has not been adopted or placed in the custody of

relatives, the child would be a ward of the state (<https://www.revisor.mn.gov/statutes/cite/260C.515>). Review Section 6 of “[CHECKLIST: Children \(HRP-416\)](#)” which details the requirements for research involving children who are wards of the state.

If the child does not have biological or adoptive parents to provide consent, refer to “[SOP: Legally Authorized Representatives, Children, and Guardians \(HRP-013\)](#).” If biological/adoptive parents are not available to consent on behalf of a minor, the study team is strongly encouraged to seek guidance from the Office of General Counsel to ensure appropriate legal authority to consent.

The Institutional Official will determine whether a research activity constitutes experimental treatment. This determination will be informed by the Office of General Counsel (in consultation with IRB staff and member(s) with relevant expertise assigned to review).

See the sections [How do I create an assent document](#) and [How do I create a parental permission document?](#) to help you determine what information to communicate to your participants and their parents. See [Appendix B-1, “Research involving children diagram”](#) to determine when minors may consent for themselves and when parents or guardians may consent on behalf of a child to participate in research.

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What if I’m doing research including adults with absent, diminished or fluctuating capacity to consent to participate in research?

If your research includes cognitively impaired adults, or adults with potentially absent, diminished or fluctuating capacity to consent, review the “[CHECKLIST: Cognitively Impaired Adults \(HRP-417\)](#)”, “[POLICY: Capacity to Consent \(HRP-110\)](#)”, “[POLICY: Research Involving Adults Under Court Jurisdiction \(HRP-111\)](#)”, “[SOP: Legally Authorized Representatives, Children and Guardians \(HRP-013\)](#)” and “[SOP: Informed Consent Process for Research \(HRP-090\)](#)” to ensure you have provided sufficient information in your protocol. The IRB recommends and may require the use of participant education materials, including the [brochures and contact cards](#).

Your protocol should specify the validated assessment tool that will be used for assessing capacity to consent to research (See [POLICY: Capacity to Consent \(HRP-110\)](#) for requirements). If the MacCAT-CR or UBACC tool will be used for assessing capacity to consent to research, the assessment record form (such as [MacCAT-CR Assessment Form \(HRP-226\)](#) or [UBACC Interview Form \(HRP-227\)](#)) does not need to be submitted as part of the IRB submission. However, the IRB may require additional documentation for other tools to determine whether the tool is appropriate in the context of the study and population.

For studies involving non-English speaking participants, the protocol should describe how the assessment will be conducted. The assessment tool does not need to be translated unless the assessor will assess the participant’s capacity to consent by speaking in the participant’s language. For studies where the assessment will be conducted in English but will include the involvement of an interpreter, the assessment tool does not need to be translated.

Your protocol should be explicit regarding the use of a legally authorized representative if one may potentially be utilized to consent on behalf of a participating adult.

As a matter of participants’ protection, assent should be obtained from incompetent or incapacitated adults for research participation to the extent they are able to provide assent. Even where a legally authorized representative has consented to the research participation, an incompetent or incapacitated adult may not be included over his or her objection (known as dissent).

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What if my research is a UMN Department of Psychiatry clinical drug trial?

Department of Psychiatry clinical drug trials require review by Advarra IRB (previously Quorum IRB Review). The above referenced required documentation for reliance on Advarra applies to Department of Psychiatry clinical drug trials. Investigators in the Department of Psychiatry conducting clinical drug trials are required to notify The Office of Ombudsman for Mental Health and Developmental Disabilities (OMHDD) within 24 hours of a U of M research participant's death or serious injury.

The [Ombudsman Reporting Transmittal Form](#) is used by HRPP and the University of Minnesota Principal Investigator to report to OMHDD pursuant to Minnesota Statute 245.92 and 245.94. Reports of death or serious injury of locally enrolled study participants in psychiatry clinical drug trials must use the Transmittal Form as the cover page to the applicable report form available on the [OMHDD website](#). Additional information on reporting can be found on the OMHDD website: <http://mn.gov/omhdd/reporting-death-or-serious-injury/>.

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What about participation of individuals with limited English proficiency, meaning non-English speakers?

It is a core principle that persons should not routinely be excluded from participation in research simply because they do not understand English. However, investigators and the IRB must carefully consider the ethical ramifications of enrolling or excluding potential participants when a language barrier exists between the investigator(s) and some or all of the potential participants. Because they may not fully understand what they are consenting too, it may not ever be appropriate to enroll a non-English speaking individual in:

- Early phase clinical trials without a prospect of direct benefit and enrolling a limited number of participants;
- Greater than minimal risk research without the prospect of direct benefit; or
- When interpreters will not be readily available throughout research participation.

Expected Encounters. If you expect or plan to enroll any individuals with limited English proficiency, you must provide certified, translated versions of the full study consent form and any key study documents in the anticipated participants' native/preferred language. See "[What translation or certification services are acceptable or required?](#)" for more information.

Unexpected Encounters. If you do not expect and do not plan to enroll any persons known to have limited English proficiency but will include such individuals should they happen to qualify for your study and express interest in participating, you may use the short form consent process with prior approval from the IRB. See "[What are the expectations for using the short form process?](#)"

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What are the expectations for using the short form process?

The short form is not a substitute for a "full length" consent form. All short-form methods must be approved by the IRB before being implemented. The short form may be used for the unexpected situation of a non-English speaking potential study participant. See "[What about participation of individuals with limited English proficiency, meaning non-English speakers?](#)"

Effective July 1, 2019, for studies that are greater than minimal risk and participant participation in the study is planned to last 30 days or more (e.g., a 5-year clinical trial), investigators must translate the full-length study consent document to the needed specific language(s). In addition, the principal investigator is responsible for ensuring that:

- The translation is certified and from a reputable translation service (See “[What translation or certification services are acceptable or required?](#)”) within 30 days of the initial consent obtained via the short-form method.
- Once certified, the translated study consent document and the certification must be submitted to the IRB for review and approval, via a Modification in ETHOS.

Once IRB approval is received, the researcher must provide a copy of the translated study consent to all participants who previously signed the short form and/or the participants' legally authorized representative.

Effective January 25, 2021, for minimal risk research or greater than minimal risk research where participation in the study is not planned to last more than 30 days, investigators do not have to translate the full-length study consent after use of the short form. However, if more than three potential participants of a specific language (e.g., French, Mandarin, Swahili) for a specific study need consent (forms) then a full-length consent form in the specific language must be developed and approved by the IRB.

See [Appendix B-4](#) for help in the understanding these requirements.

Additional Information:

- Note that the use of the short form method requires the involvement of a witness during the consent process.
- The procedures for short form consent process and documentation can be found in [SOP: Informed Consent Process \(HRP-090\)](#) and [SOP: Written Documentation of Consent \(HRP-091\)](#). Review the “[WORKSHEET: Short Form of Consent Documentation and Process \(HRP-317\)](#)”. Use “[Short Form Consent Template \(HRP-507\)](#).” You will find available translated short forms on the IRB website [HERE](#).

Both policy requirements regarding the University’s short form use and translation are applied to studies approved on or after the effective date.

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How do I document optional study participation when the short form method is used?

The investigator must obtain documentation of any optional study participation using the IRB-Approved translated study consent document or provide a plan for documenting optional study participation to the IRB for review and approval.

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What translation or certification services are acceptable or required?

Exempt research does not require certified translations and the translation can be completed by the researcher if he or she is a native speaker of the language or other appropriate mechanism. However, researchers must provide an attestation that the translation accurately depicts the study information. The attestation should be provided in the IRB submission.

Certified translations are required for non-exempt research for participant facing materials including recruitment material, consent document, etc. Investigators should consider the following when selecting a service for translation and/or certification of consent documents or key study materials:

- A. Qualifications and expertise. For example, biomedical studies should use a service that has translators with medical expertise.
- B. Credibility. Review public comments about the service prior to use.

The following are vendors (not supported or endorsed by the University of Minnesota) provide translation and certification for many languages and have medical expertise:

- BURG Translations (<https://burgtranslations.com>)
- MN Translations (<https://www.minnesotatranslations.com>)
- Tomedes (<https://www.tomedes.com/>)
- Click for Translation (<https://clickfortranslation.com/>): Provides certification of translations completed by someone other than the vendor).

If the investigator does not use a commercial vendor, a letter of certification from the translator is required. This letter should include an attestation from the translator, information about the translator's expertise as it relates to the study topic (i.e., medical expertise for biomedical research), and fluency and experience with the given language. The IRB will review this information to determine whether the translation is sufficient or a commercial service is required. A "[Certification Attestation of Translation \(HRP-574\)](#)" can be used if the translator does not have a standard letter that includes these requirements. This attestation should not reflect or state the investigator's attestation of the translation and should only be used by translators.

Be aware that there is a varying range and degree of issues that inaccurate, imprecise, and culturally incongruent translations can introduce ([Brelsford, Ruiz, Beskow, 2018](#)). There is no such thing as a perfect translation. Investigators should communicate with translators the meaning of key concepts to ensure that they are precisely conveyed in the translated materials ([Brelsford, Ruiz, Beskow, 2018](#)).

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What is the scope of my role and the role of the interpreter in the consent conversation?

The investigator is responsible for presenting the information in the English version of the study's consent document orally to the potential participant. The interpreter will interpret the investigator's presentation. The investigator is responsible for ensuring that the potential participant understands the information and should encourage questions from the participant or the legally authorized representative.

When an interpreter is used in conjunction with the full translated version of the English version of the consent form, can the medical interpreter participate by phone or videoconference?

Yes. The interpreter may participate by phone or videoconference because they are not required to sign the consent form. However, participation of the interpreter by phone or videoconference should be documented in the translated consent document and a clinic chart/progress note/other source document. The investigator should be sure that the connection is clear and that technical problems do not interfere with the consent discussion.

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When informed consent is obtained using the 'short form' written consent document, can the interpreter interpret by phone or videoconference?

Generally, no. In order to fulfill the regulatory requirements for documentation of informed consent using the 'short form' written consent document, the interpreter must be able to sign the English version of the consent form and the 'short form' written consent document in the subject's language. In situations where an interpreter is only available by phone or videoconference due to the rarity of the language or due to safety measures related to a pandemic, natural disaster, or time of national emergencies, investigators must submit a request to the IRB requesting an exception. In these situations, investigators must also provide a plan for how an interpreter will be available for future encounters with the participant during research participation.

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Is an interpreter required for future study visits or follow-up communications?

Yes. You will need to ensure that an interpreter is available for any future visits or communications with the Non-English speaking research participant. When considering the enrollment of a non-English speaker, consider carefully whether appropriate resources will be available to support their participation.

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How do I obtain HIPAA Authorization for non-English speaking participants?

Inclusion of non-English speaking participants requires the use of a standalone HIPAA Authorization. Investigators should involve an interpreter to help support the HIPAA Authorization conversation. If non-English speaking participants want to give authorization, they must sign the HIPAA Authorization form. Only the participant or the participant's legally authorized representative can sign the HIPAA Authorization. The interpreter should not sign the HIPAA Authorization unless he or she is also the participant's legally authorized representative.

The Health Information Privacy Compliance Office (HIPCO) has made available translations of the HIPAA Authorization form in the same languages of the short form consent form posted in the HRPP Toolkit Library. When HIPAA Authorization is required and the short form consent will be used to enroll a non-English speaker, the translated version of the HIPAA Authorization form must be used. [Access translations of the HIPAA Authorization Form.](#)

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Do I need to translate the HIPAA Authorization for non-English speaking participants?

Currently there is no requirement to translate the HIPAA Authorization form into other languages for non-English speaking participants. If non-English speaking participants want to give authorization, they must sign the HIPAA Authorization form.

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If re-consent is required, do I have to translate the revised study consent form?

If the study is required to use a translated full-length study consent and there is a revision to the study's consent form that requires re-consent of participants, the investigator must obtain a translation of the revised text. It is important to consider whether the prior translation is based on the most current, IRB approved consent form for the study. There may be situations where revisions to the study's consent form will not require a complete re-translation (i.e. starting over). The investigator should consult with an appropriate translation service to identify if the service can address the revisions within the existing translation of the study consent form. In doing so, investigators may reduce the cost of the "new" translation.

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Must study questionnaires, instruments, information sheets, or other participant facing materials be translated into a participant's language?

Generally, yes. Investigators are expected to provide participants with a written translation of all study documents that are given to research participants in the study to ensure that they can follow study directions and participate safely in the study.

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What if I'm doing research involving American Indian or Alaskan Native populations?

In order to recognize the autonomous authority of sovereign nations, and acknowledging the need for community awareness and permission for access, the IRB requires Tribal approval for research that is to be conducted within the jurisdiction(s) of federally-recognized American Indian and Alaska Natives (AIAN) Tribal government(s). You will need to secure approval from the Tribal Council or other agency of Tribal government to whom such authority has been delegated by the Council.

The IRB applies this requirement to all research, irrespective of funding source or rank or ethnic/racial identity of the researcher.

The form of documentation of approval may vary according to tribal requirements. In instances where more than one tribe or band is involved in the research project, separate permission from each entity may be required. Additional IRB or research committee review or approval may also be required by the Tribe. In those cases, final University IRB approval will be contingent upon Tribal approval.

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What if I'm conducting a study involving students?

Participation of students in research must be voluntary. Reasonable levels of extra credit or rewards may be offered for participating in research. If extra credit or rewards are offered for participation, students must be provided with and informed of non-research alternatives involving comparable time and effort to obtain the extra credit in order for the possibility of undue influence to be minimized. However, if participation in research is a course requirement, students must be informed of non-research alternatives involving comparable time and effort to fulfill those requirements in order for the possibility of undue influence to be minimized. Moreover, students must not be penalized for refusing to participate in research.

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Human Research Under Special Circumstances

What if my research is funded by a Federal agency?

Additional protocol requirements and PI responsibilities apply to research funded by specific federal agencies. Review “[WORKSHEET: Additional Federal Agency Criteria \(HRP-318\)](#)” and the applicable Appendix to this Manual to ensure you have provided sufficient information and understand your obligations.

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What if I'm doing a case study?

Individual case reports do not typically meet the definition of Human Research as they do not meet the “systematic investigation” or “generalizable knowledge” thresholds. Therefore, case reports generally do not

require IRB review. Report about three or fewer clinical experiences or observations identified in the course of clinical care, provided that it does not involve FDA regulated investigational products (e.g., drugs, devices, biologics). Case reports are generally done by retrospective review of medical records and highlight a unique clinical treatment, case or outcome. Please note: [UMN Health Information Privacy and Compliance Office \(HIPCO\)](#) review may still be required.

When a series of case reports is contemplated, consider whether your project meets the definition of Human Research. If you are unsure, submit in ETHOS for a determination.

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What if I'm teaching a research methods or "courseroom" class?

Research projects that occur within courses are designed to provide students an opportunity to practice various research methods such as interview, observation and survey techniques, as well as data analysis. Typically such projects are quite limited in scope and are not intended for dissemination or to contribute to generalizable knowledge.

Course-based research projects and data collection activities:

- Should not include potentially vulnerable participants or participants younger than 18 years of age;
- Should not collect or include sensitive, personal or potentially incriminating information or otherwise put participants at risk; and
- The data must be recorded anonymously (i.e., with no name, social security number, or any other code that can be linked to a participant).

These projects are considered "courseroom exercises" and are not subject to review by the IRB unless the student-investigator anticipates using the results in his or her dissertation, publishing the results or presenting at a professional meeting, or unless the faculty member expects to compile all students' results with the intention of publishing or presenting. In those situations, the student-investigator should complete the "[Human Research Determination Form \(HRP-503\)](#)" and have their faculty advisor submit the Determination Form in ETHOS and the IRB will make a determination regarding oversight requirements, if any.

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What if I'm conducting community-based participatory research (CBPR)?

The IRB supports mechanisms that allow researchers to involve community members in the research process whenever appropriate and encourages researchers to develop and establish positive relationships with the community and community members.

The IRB has experience and knowledge in the conduct and review of CBPR and understands that CBPR protocols may go through multiple changes and iterations before the research is completed and that, in most cases, researchers should plan to inform the community of the results of the research.

For more information see:

1. [Office of Public Engagement](#)
2. [Urban Research and Outreach/Engagement Center](#)
3. [Children Youth and Family Consortium](#)
4. [Office of Community Engagement for Health](#)

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What if my research involves deception?

Research which requires deception regarding the purpose of the research or any other necessary element of consent is permissible when justified by prospective scientific, educational, or applied value and when effective non-deceptive alternative procedures are not feasible. Additional consent debriefing requirements are necessary to obtain informed consent for this type of research.

You must provide a prompt opportunity for participants to obtain appropriate information about the nature, results, and conclusions of the research, and then take reasonable steps to correct any misconceptions that participants may have of which the psychologists are aware. If a participant in a study involving deception chooses to withdraw consent following the debriefing, the data collected in that case may not be included in the analysis of the study.

Deception is a form of alteration of the consent process and alteration of the consent documentation. You should review the “[CHECKLIST: Waiver or Alteration of Consent Process \(HRP-410\)](#)” to ensure that you have provided sufficient information.

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What if I'm only performing research activities as the coordinating center at the University of Minnesota?

The term ‘Coordinating Center’ (CC) covers a number of very different research-related activities that range from a data center focused on the aggregation, management, and analysis of data from multiple sites, to a study-wide center responsible for overseeing all aspects of a multi-site study. Because the nature of these activities may vary from study to study, depending in part on the design of the study and the type of funding mechanism (e.g., cooperative agreements may differ significantly from program projects), it is critical that investigators accurately describe to the IRB exactly what their responsibilities are – as detailed in the grant application or contract. It is the expectation of the IRB that those serving as a coordinating center will have adequate resources and expertise to carry out these responsibilities and have processes in place to ensure appropriate oversight.

Researchers are expected to submit a copy of the primary protocol and Local Protocol Addendum (HRP-508). [HRP-508](#) must include information specific to the responsibilities of the coordinating center and activities taking place locally. You are encouraged to submit the center’s SOPs with your application. The IRB will review the center’s standard operating procedures and determine whether the operations center or coordinating center has sufficient mechanisms in place to ensure that, where applicable, the following criteria are addressed:

- management, data analysis, and data safety and monitoring plan is adequate, given the nature of the research involved;
- sample protocols and informed consent documents are developed and distributed to each collaborating institution;
- each collaborating institution holds an applicable approved Federal Wide Assurance (FWA);
- each protocol is reviewed and approved by the IRB at the collaborating institution prior to the enrollment of subjects;
- any substantive modification by the collaborating institution of sample consent information related to risks or alternative procedures is appropriately justified; and
- informed consent is obtained from each subject in compliance with HHS regulations.

What if I'm doing research involving genetic testing and/or information?

Genetic testing is defined as the analysis of human DNA, RNA, chromosomes, proteins, and certain metabolites in order to detect heritable disease-related genotypes, mutations, phenotypes, or karyotypes.

The Minnesota Genetic Privacy Act¹ classifies genetic information as private data. The Minnesota Supreme Court has interpreted the definition of genetic information to include blood samples. Researchers must have written informed consent to collect, use, store or disseminate genetic information, including blood samples, for research.

In addition, certain protection is afforded to participants under the Genetic Information Non-discrimination Act (GINA) where protocols include genetic testing. See the “[TEMPLATE CONSENT DOCUMENT \(HRP-590\)](#)” for required language.

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What if I'm doing research with data or specimens?

According to DHHS regulations, IRB oversight is required for research use of identifiable private information or human specimens from research and/or non-research databases or repositories. Investigators may use identifiable private information or human specimens for research described in the protocol approved by the IRB.

According to FDA regulations, use of human specimens (identified or de-identified) is subject to the review and approval of the IRB. For example, research that involves the testing or evaluation of medical devices, including In Vitro Diagnostic Devices, using identified or unidentified human specimens is subject to the review and approval of the IRB.

If the proposed new use is an amendment to an already approved protocol, investigators must submit a protocol modification request for IRB review and approval.

If the proposed new use is not an amendment to an already approved protocol, investigators must submit a protocol for prospective IRB review and approval before the research may begin.

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How do I ensure an existing repository meets current regulatory requirements?

There are a number of existing stand-alone banking protocols at the University of Minnesota. It is a goal to make sure that these banking protocols meet current regulatory requirements. Considerations and possible changes investigators may need to make for maintaining an existing repository include asking and addressing the following questions:

- Is the collection or transfer of data and/or specimens ongoing or complete?
- Was/is informed consent and HIPAA authorization for banking obtained or was/is a waiver issued?
NOTE: Informed consent is the cornerstone of ethical conduct of research. The IRB will review the consent process (and HIPCO will review the HIPAA authorization or combined HIPAA and consent document) to determine if adequate information describing future research uses was/is included to permit continued release. There may be limits on how existing materials can be used/distributed.
- Does the protocol meet the current standards for repository protocols, included in [Database, Registry, Repository Protocol \(HRP-597\)](#) and reflected in [WORKSHEET: Database, Registry, and Repository \(HRP-337\)](#)?

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¹ Minn. Stat. 13.386.

What if I want to create a repository, database, or registry for research?

Rather than including banking data or specimens as part of individual research protocols, investigators should consider the development of a stand-alone protocol for the repository. In addition, investigators should consider collaborating with BioNet or the [CTSI Best Practices Integrated Informatics Core](#) rather than creating their own repository, database, or registry. Use [Database, Registry, Repository Protocol \(HRP-597\)](#) to develop the plan that meets regulatory requirements reflected in [WORKSHEET: Database, Registry, and Repository \(HRP-337\)](#). The completed protocol and any other supporting documents must be submitted in ETHOS for IRB review and approval. Also see [Appendix B-2](#) for additional information regarding IRB and HIPAA requirements.

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What if I'm doing research with controlled substances?

Investigators conducting research with controlled substances must comply with the University policy, [Using Controlled Substances for Research](#), and federal and state regulations relating to controlled substances.

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What if I'm doing research with drugs?

The Food and Drug Administration (FDA) requires that a sponsor or investigator obtain an IND from FDA for clinical investigations involving drugs or dietary supplements. If the investigation uses a marketed product, the sponsor or investigator may propose that the investigation is exempt from an IND under 21 CFR 312.2(b) which states:

- (b) Exemptions. (1) The clinical investigation of a drug product that is lawfully marketed in the United States is exempt from the requirements of this part if all the following apply:
 - (i) The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug;
 - (ii) If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product;
 - (iii) The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
 - (iv) The investigation is conducted in compliance with the requirements for institutional review set forth in part 56 and with the requirements for informed consent set forth in part 50; and
 - (v) The investigation is conducted in compliance with the requirements of 312.7. [regarding marketing and promotion]

Criteria (i), (ii), and (v) are under the control of the IND sponsor, and the U of M holds the sponsor responsible for complying with those criteria. Criterion (iv) is satisfied with review by the U of M IRB or an IRB with which the University of Minnesota IRB has a reliance agreement.

The U of M will consider whether the conditions for (iii) are met, and will send a written communication via the ancillary review process in ETHOS to the investigator or sponsor-investigator and the IRB addressing that item.

A written statement in the protocol should be included, indicating that all the criteria for IND exemption have been met.

For cases where the use of the drug is not identical to that described in the FDA approved labeling, provide a rationale explaining how the research does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the product.

For clinical investigations using a dietary supplement, the IRB will require that the sponsor of the investigation obtain an IND if the clinical investigation is intended to evaluate the dietary supplement's ability to diagnose, cure, mitigate, treat, or prevent a disease. The IRB will accept a written statement from the FDA that an IND is not necessary for a given clinical investigation of a dietary supplement.

University of Minnesota researchers are also required to follow the policy Using Legend and Investigational Drugs for Clinical Research <https://policy.umn.edu/research/investigationaldrugs>. This policy requires, among other items, investigators to either contact Fairview Investigational Drug Services (Fairview IDS) for full services or enroll in a "Registered Only" status using the IDS Registration Only (RO) Form. Researchers who select the RO process bear full responsibility for ensuring the safe storage of their drugs.

Fairview Research Administration is responsible for providing researchers with the Fairview IDS identification number as part of their ancillary review and approval correspondence. Investigators are responsible for entering the Fairview IDS identification number into the appropriate study protocol in ETHOS. The IRB will not finalize approval of a protocol until after receipt of the Fairview Research Administration approval.

If your protocol involves the use of drugs, biologics or tobacco products, review "[WORKSHEET: Drugs \(HRP-306\)](#)", and "[Appendix A-2: Additional Requirements for FDA-Regulated Research](#)" of this Manual to ensure you have provided sufficient information.

Submit a copy of each of the following with your protocol:

- Investigator's Drug Brochure*
- Background Information for Food Supplements*
- Documentation from sponsor or FDA verifying the IND (Investigational New Drug) number if one is required for the research.

* If an IND is not required, provide the reason why in writing.

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What if I'm doing research with devices?

The FDA regulations place additional requirements on the IRB for the review of studies using medical devices. Before reviewing research involving devices, the IRB must identify and evaluate the regulatory status of the device study such as:

- Whether the device study qualifies as a Non-Significant Risk (NSR) IDE study,
- Whether the device study qualifies as a Significant Risk (SR) IDE study, or
- Whether the research use of the device is exempt from the IDE regulations.

If you believe the device is NSR IDE and the IRB agrees, then the IRB may go on to review the research. If the IRB disagrees and finds the study to be SR IDE and there is no FDA IDE exempt determination is provided, the IRB will provide the investigator and/or sponsor with that finding. The sponsor is responsible for notifying the FDA of the IRB's SR IDE determination. The IRB will not review the research until the sponsor provides written proof that either:

- The FDA has granted an IDE to the sponsor, or

- The FDA disagrees with the IRB’s SR IDE determination and has determined that the device is NSR IDE

If the FDA has not responded to an IDE application, as described in FDA 21 CFR 812.30, this proof may consist of a letter showing that an IDE application was acknowledged by the FDA at least 30 days prior to the date on which the submission was forwarded to the IRB.

If the research is SR IDE, provide the IRB with proof of the IDE number at the time of submission. In most cases, submitters should ensure the IRB receives a copy of the IDE letter that has not been redacted. Redacted IDE letters generally do not provide sufficient information for the IRB.

If a participant in the study must undergo a medical procedure as a part of the study, and that medical procedure is not one which the participant would otherwise undergo as part of standard medical care, the IRB must consider the risks associated with the procedure as well as the use of the device. If potential harm to subjects could be life-threatening, could result in permanent impairment of body function, or permanent damage to body structure, the device should be considered SR IDE.

If approved devices will be used as part of the research you may be asked to confirm that the devices will be used within their approved labeling.

If your protocol involves the use of a device review “[WORKSHEET: Devices \(HRP-307\)](#)” and “[Appendix A-2: Additional Requirements for FDA-Regulated Research](#)” of this Manual to ensure you have provided sufficient information.

Submission requirements for device research include providing a device manual (also called “Instructions for Use”) and ONE of the following:

- Unredacted FDA Letter granting the Investigational Device Exemption (IDE);* OR
- Letter from sponsor stating that the study is a non-significant risk IDE device study and the basis for that determination;* (unredacted); OR
- Documentation of why the investigation is exempt from the IDE requirements under 21 CFR § 812.2(c) (such as the PMA approval letter/number or 510(k) clearance letter/number) or otherwise exempt.*

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What if I want to use a Humanitarian Use Device?

Humanitarian Use Devices have been granted a special exemption by the FDA known as a Humanitarian Device Exemption (HDE). The expected market for HUDs is so small that studies needed for full FDA approval would never be able to be carried out.

1. Using an HUD for its Approved Indication

The use of a HUD for its approved indication does not constitute “research” as long as you are not collecting safety or effectiveness data. Although it is not considered as “research” IRB review and approval is required by FDA regulations before clinical use of an HUD at a facility.

So long as you intend to use the HUD for clinical care within its approved indication and you do NOT plan to evaluate the safety or effectiveness of the device, you should review the “[WORKSHEET: Criteria for Approval for HUD Use in Clinical Care \(HRP-323\)](#)” and submit the [HUD Protocol \(HRP-596\)](#) in ETHOS.

Use of a HUD in this manner is not considered “research”, the IRB’s education requirement, as well as the requirement for independent scientific assessment of the protocol and for the use of a research-specific HIPAA authorization form, are waived.

The patient information booklet must be included in the ETHOS submission. This patient information booklet should make clear that the physician believes this device might work better than standard therapy but that it has not been tested in the usual way for full FDA approval the way most devices are since its use is rare.

As the use of a HUD for clinical care is not research, and the HUD is a legally marketed device, the IRB does not make a significant risk or non-significant risk determination. Continuing review may take place via expedited review or by review of the full convened committee.

2. Using and HUD beyond its Approved Indication (Investigational Use)

Clinical investigation of an HUD beyond its approved indication requires an approved Investigational Device Exemption (IDE). Physicians may collect safety and effectiveness data to support a Pre-Market Approval (PMA) for the HDE-approved indication without an IDE as long as the HUD is used in accordance with its approved indication.

If the HUD is being used in the context of a clinical investigation, a completed IRB application is required, to include a research-specific HIPAA Authorization. All University and IRB investigational device-related policies and procedures apply to an HUD that is being used in the context of a clinical investigation. Review the “[WORKSHEET: Devices \(HRP-307\)](#)” to ensure you have provided sufficient information.

See FDA guidance titled “[Guidance for HDE Holders, Institutional Review Boards \(IRBs\), Clinical Investigators, and Food and Drug Administration Staff Humanitarian Device Exemption \(HDE\) Regulation: Questions and Answers](#)” for more information about requirements for use of HUDs.

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What if I am the sponsor or sponsor-investigator of an IND or IDE?

You are required to follow FDA regulations that apply to your research.

If you are employed by the University of Minnesota you are also required to follow the requirements in the policy Reporting Sponsor-Investigator IND/IDE and FDA Pre-Submissions <https://policy.umn.edu/research/indide>. Submit Form UM 1813 to the HRPP Central File as discussed in the [policy](#).

Direct questions about any of these requirements to medreg@umn.edu.

You are also required to comply with ICH GCP for drugs, biologics and as applicable to devices.

The IRB complies with International Council for Harmonisation Good Clinical Practice E6 (ICH-GCP E6) guidelines for all research to the extent that they are compatible with FDA and DHHS regulations. The IRB will comply with ICH-GCP E6 in one or both of the following circumstances:

1. PI indicates the sponsor requires following ICH-GCP E6 standards; and/or
2. Sponsored Projects Administration (SPA) confirms it is a contractual requirement to follow ICH-GCP E6 standards.

Review “[Appendix A-3: Additional Requirements for Clinical Trials \(ICH-GCP\)](#)” in this Manual for additional study requirements and investigator responsibilities specific to these studies.

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What if the FDA requires that a long-term follow-up (LTFU) be conducted for my human gene therapy (GT) study?

To understand and mitigate the risk of a delayed adverse events, subjects in gene therapy trials may be monitored for an extended period of time, which is commonly referred to as the “long term follow-up” (LTFU)

period (of a clinical study). LTFU observations are extended assessments that continue some of the scheduled observations of a clinical trial past the active follow-up period, and are an integral portion of the study of some investigational GT products.

Complete and submit a [Biomedical Protocol \(HRP-590\)](#) to the IRB for review and include all supporting documents. If the sponsor has already developed a protocol, submit the sponsor's protocol and a [Local Protocol Addendum \(HRP-508\)](#) to document what procedures will occur locally. While administration of the investigational GT product is not part of the LTFU study, the IRB considers these studies to be greater than minimal risk and require full committee review. As these studies are also conducted under an IND, the ETHOS SmartForm and [Biomedical Protocol \(HRP-590\)](#) should include information regarding the investigational product.

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What if I need expanded access to investigational drugs, biologics, and devices?

Sometimes called “compassionate use”, **expanded access** is a potential pathway for a patient with an [immediately life-threatening condition or serious disease or condition](#) to gain access to an [investigational medical product](#) (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available.

FDA has set up several methods to access investigational drugs, biologics, and devices. The agency has outlined those methods for Expanded Access here:

<https://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm>. Also, see IRB SOPS for additional details regarding IRB review steps.

Helpful guidance regarding FDA requirements can be found at the following web links:

DRUG – FDA guidance regarding access to Investigational drugs for Treatment Use (pre-use):

1. [“Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers,”](#)
2. [“Charging for Investigational Drugs Under an IND – Questions and Answers,”](#) and
3. [FDA form 3926 Individual Patient Expanded Access Investigational New Drug Application](#)

DEVICE – FDA guidance regarding access to investigational devices for treatment use (prior to use):

- FDA has provided guidance on expanded access for medical devices at <https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm051345.htm>

For questions about and requests for emergency use and expanded access for drugs, biologics, devices or to get an emergency IND or IDE, contact FDA at:

- During Normal Business Hours (8 a.m. - 4:30 p.m. ET, weekdays):
 - Drugs: 301-796-3400 [CDER's Division of Drug Information]
 - Biologics: 800-835-4709 [CBER's Office of Communication, Outreach and Development]
 - Devices: 301-796-7100 [CDRH's Division of Industry and Consumer Education]
- Nights/Weekends: (866) 300-4374 [Office of Crisis Management & Emergency Operations Center]

The table below outlines the submission processes for each category of expanded access and emergency use of drugs, biologics and devices. The University of Minnesota follows requirements outlined by FDA when evaluating these uses.

Expanded Access (including Emergency Use) IRB Application Quick Reference Guide

Submission Type	Submission Process
Emergency Use of Drugs, Biologics and Devices	<p>-Complete the Expanded Access Survey at the following link: https://umn.qualtrics.com/jfe/form/SV_cVemhWUFxFXzicJ.</p> <p>-Ensure all required sections of HRP-322 WORKSHEET EMERGENCY USE are documented and provided with your expanded access survey submission.</p> <p>-Provide a copy of the consent template using HRP-506 EMERGENCY USE TEMPLATE CONSENT DOCUMENT. Any exception to the requirements of informed consent will be evaluated using criteria included in HRP-322 WORKSHEET EMERGENCY USE.</p> <p>-Redact patient identifiers from your submission.</p> <p>-Provide the IRB with a follow-up report within 5 business days of the use by submitting the Expanded Access Survey https://umn.qualtrics.com/jfe/form/SV_cVemhWUFxFXzicJ</p> <p>If IRB concurrence was not obtained prior to the emergency use, ensure that your follow up report documents how criteria included in the HRP-322 WORKSHEET EMERGENCY USE were met.</p>
Compassionate use of Device	<p>-Complete the Expanded Access Survey at the following link: https://umn.qualtrics.com/jfe/form/SV_cVemhWUFxFXzicJ.</p> <p>-Ensure all required sections of HRP-325 WORKSHEET COMPASSIONATE USE OF AN UNAPPROVED DEVICE are documented and provided with your expanded access survey submission.</p> <p>-Provide a copy of the consent template. If a consent template does not exist, use HRP-506 EMERGENCY USE TEMPLATE CONSENT DOCUMENT and replace references to drugs/biologics, and emergency use, with “device” and “compassionate use”.</p> <p>-Redact patient identifiers from your submission.</p> <p>-Submit a follow-up report to the IRB via the Expanded Access Survey: https://umn.qualtrics.com/jfe/form/SV_cVemhWUFxFXzicJ</p>
Individual Patient Expanded Access of drug or biologic,	<p>A physician submitting an Individual Patient Expanded Access IND using Form FDA 3926 may select the appropriate box on that form (10 b) to request a waiver under § 56.105 of the requirements in § 56.108(c), which relate to full IRB review. FDA concludes that such a waiver is appropriate for individual patient expanded access INDs when the physician obtains concurrence by the IRB chairperson or another designated IRB member BEFORE treatment use begins. A physician submitting an individual patient expanded access IND using Form FDA 1571 may include a separate waiver request with the application.</p> <p>Follow steps listed in “Submitting Your Study for Review” section and ensure that the completed FDA form 3926 Individual Patient Expanded access Investigational New Drug Application (IND) waiver requested under 10b is</p>

	<p>submitted with your protocol or documentation of FDA approval of an alternate IRB approval pathway.</p> <p>-Add comment via ETHOS requesting Designated Review of the individual patient expanded access submission.</p> <p>Your submission will be assigned to a designated reviewer. Do not proceed with the use until concurrence from the designated reviewer is obtained.</p> <p>Individual patient expanded access submissions are subject to continuing review requirements.</p>
Intermediate-Size Patient Populations and Treatment INDs	<p>Follow steps listed in “Submitting Your Study for Review” section.</p> <p>Convened IRB review and approval is required. The requirement for scientific review will be assessed by the convened IRB.</p>

What if I need to request approval for a planned exception to my protocol?

A protocol exception is a one-time, intentional action or process that departs from the IRB approved study protocol for one participant. Protocol exceptions must be approved by the IRB prior to implementation of the exception. A departure from the protocol that is submitted to the IRB after the action or process has occurred is considered Non-Compliance that must be reported to the IRB as new information.

To submit an exception request, investigators must submit a Modification in ETHOS (or a Change in Protocol Request if the study for which the request is being made has not yet been migrated to ETHOS) since such a request is considered a modification to previously approved research. The following information must be submitted with the Modification (or Change in Protocol Request) for an exception:

- Documented approval from the study sponsor, medical monitor and other oversight entities (e.g., FDA for studies under an IND or IDE held by a University sponsor) as applicable;
- A description of the requested exception including references to the approved protocol, proposed date, rationale, clarification as to why the change/action is one time and any plans for communicating the exception to the participant;
- Assessment of increased risk involved in the exception;
- Assessment of participant benefit from the exception;
- Revised consent form, if applicable;
- Assessment of exception impact on data integrity – including a statement about whether or not the data collected as a result of the exception will be analyzed in a different manner from other collected data; and
- Declaration of time sensitivity and applicable rationale.

Factors that may influence IRB review of an exception include submission of a revised consent or addendum to the consent form and/or plans to modify the protocol.

The IRB will, within IRB standard operating procedures, accommodate exception requests as quickly as possible. For time-sensitive matters, add a comment regarding the time-sensitivity to the ETHOS submission and select “IRB Coordinator” under Question 3, “Who should receive notification?” Exceptions will be reviewed by non-committee review or by a convened IRB depending on the nature of the request. Generally, the IRB will review the modification via non-committee review when a modification meets the following criteria:

- Does not affect the design of the research,
- Does not add more than minimal risk to participants, and
- Falls into one of the federal expedited review categories.

When immediate action must be taken to eliminate an apparent, unexpected hazard to the research participant, the PI may act without prior IRB approval. In these cases, the PI must report the situation to the IRB within 5 business days by submitting a Report of New Information.

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What if I'm using human embryos or human embryonic stem cells?

You must follow University policies for the use of human embryo or human embryonic stem cells in research, including [Conducting Research with Human Embryos or Embryonic Stem Cells](#).

To the extent an embryonic research study requires review and approval by the IRB, review will be conducted by the full convened IRB. The IRB will consider limiting the scope of the study to a small number of subjects in the earliest stages of this research and will assign frequent reporting and continuing review intervals for this research.

The IRB will coordinate its review of this research with the Research Intelligence and Compliance Team and other institutional offices, including communications entities.

The IRB, through the Executive Director of the HRPP, will officially notify the Institutional Official that this research has been proposed and is under review.

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What if I'm using human fetal tissue in transplantation?

You must follow all federal, state and University policies, laws, and regulations concerning the use of human fetal tissue in transplantation, including [Procuring and Using Human Fetal Tissue for Transplantation Research](#).

First, you submit an application to the Fetal Tissue Research Committee (FTR) for review and approval to use human fetal tissue in research. If FTR approval is granted, then submit an application for IRB approval, the IRB will follow all requirements related to donation of tissue, designation of recipient, and all specific requirements for informed consent of all parties.

Review of this research is to be conducted by the full convened IRB. The IRB will consider limiting the scope of the study to a small number of subjects in the earliest stages of this research.

The IRB will assign frequent reporting and continuing review intervals for this research.

The IRB, through the Executive Director of the HRPP, will officially notify the Institutional Official that this research has been proposed and is under review.

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What if I'm using human fetal tissue in NON-transplantation research?

You must follow Minnesota law (Minnesota Statute 137.47) and all University policies for the use of human fetal tissue in research, including [Acquisition, Use, and Disposition of Donated Human Fetal Tissue for research \(Non-Transplantation\) or Teaching](#).

Application to the IRB is not required unless you interact with, or receive identifiable information about the donor of the tissue, or if the research meets other criteria for IRB review. If the research does not meet the

criteria for review by the IRB, then the IRB's role is limited to reviewing Fetal Tissue Research Committee decisions to ensure all alternatives have been considered.

What if I'm doing research with potentially hazardous biological agents (including Human Gene Transfer)?

The Institutional Biosafety Committee (IBC) reviews University research involving recombinant or synthetic nucleic acid molecules (r/sNA), infectious agents, or biologically-derived toxins. r/sNA activities include but are not limited to r/sNA transfer into organisms (including human gene transfer), generation and/or use of infectious agents as vectors for r/sNA transfer, and generation and/or use of engineered agents/organisms. Biologically-derived toxins are those having high acute toxicity (i.e., a mammalian LD50 of less than or equivalent to 100 micrograms/kg body weight) or significant potential for serious subacute or chronic toxicity (e.g., carcinogenicity).

Human gene transfer (HGT) is the deliberate transfer into human research participants of either:

- Recombinant nucleic acid molecules, or DNA or RNA derived from recombinant nucleic acid molecules, or
- Synthetic nucleic acid molecules, or DNA or RNA derived from synthetic nucleic acid molecules that meet any one of the following criteria:
 - a. Contain more than 100 nucleotides; or
 - b. Possess biological properties that enable integration into the genome (e.g., cis elements involved in integration); or
 - c. Have the potential to replicate in a cell; or
 - d. Can be translated or transcribed.

Research cannot be initiated until IBC (of the clinical trial site), IRB, and all other applicable institutional and regulatory authorization(s) and approvals have been obtained. All HGT clinical trials are subject to FDA regulations as biological products. The consent form for human subjects must meet the requirements of 45CFR46.116 and 21CFR50.25 for informed consent.

Researchers may submit applications simultaneously to the IRB and IBC. HRPP staff may triage and pre-review the applications. The IBC performs a risk assessment of the research activities focused on biosafety issues (e.g., administration, shedding) and is tasked to eliminate or reduce the potential exposure of potentially hazardous biological agents to University personnel and the environment.

An individual patient expanded access IND, including emergency use, is not research subject to the NIH Guidelines and thus does not need to be submitted to an IBC, if the following conditions are met:

- a PI is submitting an individual patient expanded access IND using Form FDA 3926;
- the PI selects the appropriate box on that form to request a waiver under 21 CFR 56.105 of the requirements in 21 CFR 56.108(c); and
- the FDA concludes that such a waiver is appropriate.

Review the “[WORKSHEET: Ancillary Review Requirements \(HRP-309\)](#)” to understand the process for ancillary review.

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What if I'm doing international research?

Your protocol must include a description of the international or local immigrant research location and describe the levels of protection appropriate for the location (i.e., appropriate access, consent options, etc.). In addition, for drug and device studies, investigators are responsible for providing documentation regarding compliance

with foreign regulatory oversight bodies. The University of MN IRB prefers that in international research there be a local IRB or other review committee that oversees the research in addition to the University of Minnesota in order to help ensure that the research is culturally acceptable.

Review the “[WORKSHEET: International Research \(HRP-336\)](#)” for further guidance on developing an international research protocol.

The convened IRB or designated reviewer may review and/or consult with University, local or national experts to determine if the research is appropriate based on the laws and knowledge of the country or community in which the research will take place and may consult the OHRP website publication, [The International Compilation of Human Research Protections](#), for in-country research information.

During IRB review, researchers are informed of University policies on travel approval and registration with the UMN Global Programs and Strategy Alliance through the International Travel Risk Assessment and Advisory Committee (ITRAAC). Student-investigators and faculty leading students must get approval through ITRAAC before final IRB approval will be granted.

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IRB Review of Human Research

What are the different regulatory classifications that research activities may fall under?

Submitted activities may fall under one of the following four regulatory classifications:

- **Not Human Research:** Activities must meet the university definition of “Human Research” to fall under IRB oversight. Activities that do not meet this definition of are not subject to IRB oversight or review. Review the IRB Office’s “[WORKSHEET: Human Research \(HRP-310\)](#)” for reference. Contact the IRB Office in cases where it is unclear whether an activity is Human Research.
- **Exempt:** Certain categories of Human Research may be exempt from regulation but require IRB review. It is the responsibility of the university, not the investigator, to determine whether Human Research is exempt. Review the IRB Office’s “[WORKSHEET: Exemption \(HRP-312\)](#)” for reference on the categories of research that may be exempt.
- **Review Using the Expedited Procedure:** Certain categories of non-exempt Human Research may qualify for review using the expedited procedure, meaning that the project may be approved by a single designated IRB reviewer, rather than the convened board. Review the IRB Administration’s “[WORKSHEET: Eligibility for Review Using the Expedited Procedure \(HRP-313\)](#)” for reference on the categories of research that may be reviewed using the expedited procedure.
- **Review by the Convened IRB:** Non-Exempt Human Research that does not qualify for review using the expedited procedure must be reviewed by the convened IRB.

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What are the decisions the IRB can make when reviewing proposed research?

The IRB may approve research, require modifications to the research to secure approval, table research, or disapprove research:

- **Approval:** Made when all criteria for approval are met. See “[How does the IRB decide whether to approve Human Research?](#)” below.

- **Modifications Required to Secure Approval:** Made when IRB members require specific modifications to the research before approval can be finalized.
- **Tabled:** Made when the IRB cannot approve the research at a meeting for reasons unrelated to the research, such as loss of quorum. When taking this action, the IRB automatically schedules the research for review at the next meeting.
- **Deferred:** Made when the IRB determines that the board is unable to approve research and the IRB suggests modifications that might make the research approvable. When making this motion, the IRB describes its reasons for this decision, describes modifications that might make the research approvable, and gives the investigator an opportunity to respond to the IRB in person or in writing.
- **Disapproval:** Made when the IRB determines that it is unable to approve research and the IRB cannot describe modifications that might make the research approvable. When making this motion, the IRB describes its reasons for this decision and gives the investigator an opportunity to respond to the IRB in person or in writing.

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How does the IRB decide whether to approve Human Research?

The criteria for IRB approval can be found in the “[WORKSHEET: Exemption and limited IRB Review \(HRP-312\)](#)” for exempt Human Research and the “[WORKSHEET: Criteria for Approval \(HRP-314\)](#)” for non-exempt Human Research. The latter worksheet references other checklists that might be relevant. All checklists and worksheets can be found in the [HRPP Toolkit Library](#) on the IRB Website.

These checklists are used for initial review, continuing review, and review of modifications to previously approved Human Research.

You are encouraged to use the Checklists to write your Investigator Protocol in a way that addresses the criteria for approval.

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Does the IRB have guidelines regarding risk levels of common research related medical procedures?

Yes, there is general agreement about the nature of risk from some common procedures. While the UMN IRB works to maintain consistency across its committees and expedited reviewers, the proposed participant population, the setting and the persons conducting the research vary and therefore, the IRB may come to different conclusions about the risk of the same procedure for different studies.

- **IV catheter insertion:** Generally, the IRB considers IV insertion to be minimal risk whether for infusion or for use for multiple blood draws (e.g., a PK study). However, the protocol should address the number of insertion attempts that will be permitted, the skill of the individuals placing the catheter and efforts to mitigate participant discomfort (e.g., use of topical anesthesia).
- **Skin Biopsy:** Skin biopsies are not on the list of procedures that may be reviewed using expedited procedures. Therefore, research studies implementing skin biopsy procedures will be reviewed by convened committee.
Depending on the collection site(s) (e.g. non-facial, non-genital, etc.), skin biopsies in children and adults that are limited to two millimeters or less that do not require sutures are generally considered by the UMN IRB to be minimal risk.
- **Other Biopsies:** When tissue or marrow biopsies are obtained for research-only purposes, the full board of the IRB must review the risks.

- General Anesthesia and Sedation: The IRB considers research specific use of sedation and general anesthesia to be greater than minimal risk.
- Prolongation of the duration of sedation and general anesthesia may be considered greater than minimal risk, depending on the duration and clinical circumstances.
- Gadolinium or Other Contrast Agents: The IRB has determined that use of IV contrast agents for research procedures are greater than minimal risk.
- Radiology Procedures Involving Ionizing Radiation: Exposures to ionizing radiation of up to 100 mrem/year (1mSv) is generally considered minimal risk.
- Exercise Procedures: Factors the IRB considers during the risk assessment include intensity of the exercise intervention (sub-maximal versus maximal), characteristics of population (e.g. athletes versus non-athletes), muscle groups involved, and anticipated level of fatigue, if any. For interventions involving children, the IRB would compare the intervention to what would typically occur during recess or physical education classes when assessing risk level.

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How does the IRB decide whether Human Research requires continuing review?

Under the revised Common Rule (2018 Rule), continuing review is not required for:

1. Research that is eligible for expedited review,
2. Exempt research conditioned on limited IRB review,
3. Research that has completed all interventions and now only includes analyzing data, even if the information or biospecimens are identifiable,
4. Research that has completed all interventions and now only includes accessing follow-up clinical data from clinical care procedures.

The elimination of continuing review under the circumstances above only apply to studies that are subject to the 2018 Rule. This does not apply to studies under the pre-2018 Rule as the University will not transition pre-2018 approved studies to the 2018 Rule at this time.

Non-exempt studies that are subject to FDA oversight (regardless of the level of risk), conducted or supported by the Department of Justice (DOJ), or the Consumer Product Safety Commission (CPSC), will require continuing review as these agencies do not follow the revised Common Rule requirements as of date.

In addition, the IRB can require continuing review for minimal risk research, as long as the IRB documents the decision and the rationale for this decision. The IRB will make these determinations on a case-by-case basis, and may consider:

1. Previous determinations of serious or continuing non-compliance
2. Studies with additional regulatory oversight (e.g., conflicts of interest, international research in some cases)
3. Studies subject to single IRB review where UMN IRB is serving as the sIRB
4. Studies with new findings that require additional oversight (e.g., UPIRTSO)

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What does the IRB consider when conducting a continuing review?

The IRB assumes that the criteria for IRB approval are still met at the time it conducts a continuing review. However, there may be new information that the IRB has received due to changes in policies, regulations, or investigator conduct that could alter the IRB's prior determination that would require a clarification or revision. For example, investigators may be required to adhere to a new University policy or research

regulation at the time of continuing review. In addition, the IRB may identify inconsistencies between the protocol and consent form. The IRB will also evaluate whether the investigator is following the data and safety management plan.

Changes to consent forms at the time of continuing review will be limited to situations where there are missing elements of consent that are required by the regulations and at the time of the review, the study is still enrolling research participants or participants are still participating in study activities that are related to the elements that were missed.

For more information about how the IRB will evaluate a study at the time of continuing review, see Section 5 of [WORKSHEET: Criteria for Approval \(HRP-314\)](#). More information can also be found in the OHRP Guidance, [Continuing Review](#).

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May I attend the IRB meeting at which my submission is reviewed?

It is at the discretion of the committee to determine if the PI or Co-investigator's participation at the meeting is warranted. PIs or Co-investigators may make themselves available to participate by phone. The PI or Co-investigator will be contacted if the IRB contemplates a determination to defer, disapprove, require a for-cause audit, suspend or terminate, serious non-compliance or continuing non-compliance. The IRB will attempt to call the PI during the meeting to share information about IRB consideration of the deficiency or issue identified by or reported to the IRB and give the PI an opportunity to provide any other information that could assist the IRB.

The IRB will contact you via ETHOS when your submission is assigned for full committee review. The communication will include the date and time of the meeting. Meetings typically last two hours. If you or a co-investigator listed on the study will be available, indicate that via a comment on the study in ETHOS. Please provide the name and phone number of the individual the committee should contact.

Final determinations will not be shared during the call. The study team will be notified of the review outcome in writing after the meeting.

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What will happen after IRB review?

The IRB will provide you with a written decision indicating that the IRB has approved the Human Research, requires modifications to secure approval, or has disapproved the Human Research.

1. If the IRB has approved the Human Research: The Human Research may commence once all other university approvals have been met. IRB approval is usually good for a limited period of time which is noted in the approval letter.
2. If the IRB requires modifications to secure approval and you accept the modifications: Make the requested modifications and submit them to the IRB. If all requested modifications are made, the IRB will issue a final approval. Research cannot commence until this final approval is received. If you do not accept the modifications, write up your response and submit it to the IRB.

Researchers must respond to requests from the IRB within 30 days of notices being sent. Failure to do so may cause your submission to be administratively withdrawn or discarded. Submissions that are withdrawn are returned to "pre-submission," and can be resubmitted once all of the requested modifications are made. Withdrawn studies retain all their ancillary reviews, and IRB review resumes where it was left off once the study is resubmitted. Submissions that are discarded must be resubmitted

for IRB review, and will be re-reviewed as if it is a new study. Submissions in the “Clarifications Requested - Pre-review” and “Clarification requested - Designated Review” states will be withdrawn after 30 days. Submissions in a “Modifications Required” state cannot be withdrawn in ETHOS, and may be discarded if the required modifications are not made in 30 days.

If circumstances prohibit investigators from responding within 30 day, please add a comment in ETHOS and tag the IRB Coordinator to request an extension. The IRB rarely grants more than one extension per study. Additional requests for extension will only be considered with approval of your research dean. This approval must be submitted with subsequent extension requests. Contact your research dean for information regarding how to submit a request for additional extensions.

3. If the IRB defers the Human Research: The IRB will provide a statement of the reasons for deferral and suggestions to make the study approvable, and give you an opportunity to respond in writing. In most cases if the IRB’s reasons for the deferral are addressed in a response to the deferral, the Human Research can be approved. For deferrals, investigators will be expected to follow the same timeline for required responses and requests for extensions as noted in Item 2 above.
4. If the IRB disapproves the Human Research: The IRB will provide a statement of the reasons for disapproval and give you an opportunity to respond in ETHOS.

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What if I disagree with the IRB’s decision?

Researchers may request that the IRB reconsider a decision by submitting a written response to the IRB in ETHOS within 5 business days. When submitting a request to reconsider, the researcher must provide rationale for the request, including any additional supporting documents.

Grounds for a request are limited to:

- New information not reasonably available during the IRB review/investigation
- Material failure by the IRB to follow IRB policies and procedures
- The sanction exceeds the severity of the non-compliance violations, if applicable
- The action is disproportionate to the risks to subjects safety/welfare

Documents can be included in the Supporting Documents section of the ETHOS SmartForm.

These considerations also apply to all other submissions, including Modifications, Continuing Reviews, Reports of New Information, and also where the IRB has suspended or terminated the Human Research.

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What are my obligations after receiving a Not Human Research Determination?

IRB approval is required when a research project meets the regulatory definition of human subjects research. If you have submitted a Determination Form and have received a “Not Human Research” determination, the IRB has evaluated the information you have provided, found it did not meet the regulatory definition and does not require additional IRB review or IRB approval. It is important to understand that you may have other University obligations and requirements. A “Not Human Research” determination is not equivalent to IRB approval and is not confirmation that your project has been ethically designed. You are ultimately responsible for ensuring that you understand or have anticipated any ethical concerns related to your project and that you have taken the appropriate steps to eliminate, mitigate or manage those concerns.

The IRB does not require changes in personnel to be submitted for studies that have received a “Not Human Research” determination. However, if you make significant changes to your study design proposed you may want to submit an updated determination form via a new study submission. This can be done by cloning or copying the existing ETHOS submission (see [Job Aid: How to Copy a Submission](#)). In some circumstances, the significant changes may lead to a different determination.

A “Not Human Research” determination is not the same as being Exempt. “Exempt” has a specific regulatory meaning.

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What are my obligations after receiving an Exempt determination?

If you have received a “Exempt” determination, you are not required to submit a continuing review report or minor changes to your research. You are responsible for reporting the following:

- Changes in study personnel – all study personnel must be listed on your ETHOS application and are required to complete human research training
- Significant changes to study design – significant changes to your study design must be submitted to determine if your research continues to fall within the regulatory definition of “Exempt”.
- Study closure – You must notify the IRB when your research is complete so that your study record can be closed.

It is your responsibility to understand and comply with any other University, MHealth Fairview or Gillette obligations and requirements.

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What are my obligations after IRB approval?

- 1) Do not start Human Research activities until you have the final IRB approval letter.
- 2) Do not start Human Research activities until you have obtained all other required institutional approvals, including approvals of departments or divisions that require approval prior to commencing research that involves their resources (see [WORKSHEET: Ancillary Review Matrix \(HRP-309\)](#))
- 3) Ensure that there are continued adequate resources to carry out the research safely. This includes, but is not limited to, sufficient investigator time, appropriately qualified research team members, equipment, and space.
- 4) Ensure that Research Staff are qualified (e.g., including but not limited to appropriate training, education, expertise, credentials, protocol requirements and, when relevant, privileges) to perform procedures and duties assigned to them during the study.
- 5) Ensure that the Research Staff obtaining informed consent are using the most current, IRB approved-stamped consent form. The stamped consent form is located in ETHOS in the “Final” column of the Documents tab as a PDF. This does not apply to exempt research as the consent form will not be stamped by the IRB.
- 6) Personally conduct or supervise the Human Research. Recognize that the investigator is accountable for the failures of any study team member.
 - a) Conduct the Human Research in accordance with the relevant current protocol as approved by the IRB, and in accordance with applicable federal regulations and local laws.

- b) When required by the IRB ensure that consent or permission is obtained in accordance with the relevant current protocol as approved by the IRB.
 - c) Do not modify the Human Research without prior IRB review and approval unless necessary to eliminate apparent immediate hazards to subjects.
 - d) Protect the rights, safety, and welfare of subjects involved in the research.
- 7) Submit to the IRB:
- a) Proposed modifications as described in this manual. (See “[How do I submit a modification?](#)”)
 - b) A continuing review application as requested in the approval letter. (See “[How do I submit continuing review?](#)”)
 - c) A continuing review application when the Human Research is closed even if the study does not have a continuing review requirement. (See “[How Do I Close Out a Study?](#)”)
- 8) Complete the Reportable New Information (RNI) SmartForm in ETHOS and submit within 5 business days for any required reporting (see [SOP: New Information \(HRP-024\)](#) and [WORKSHEET: Review of Information Items \(HRP-321\)](#)).
- 9) Submit an updated disclosure of financial interests within thirty days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new financial interest.
- 10) Do not accept or provide payments to professionals in exchange for referrals of potential subjects (“finder’s fees.”)
- 11) Do not accept payments designed to accelerate recruitment that were tied to the rate or timing of enrollment (“bonus payments.”)
- 12) See additional requirements of various federal agencies in [Appendix A](#). These represent additional requirements and do not override the baseline requirements of this section.
- 13) If the study is a clinical trial and supported by a Common Rule agency, one IRB-approved version of a consent form that has been used to enroll research participants must be posted on ClinicalTrials.gov, a public federal website designated for posting such consent forms by the awardee or the federal department or agency component conducting the trial. The form must be posted after recruitment closes and no later than 60 days after the last study visit.

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How do I document consent?

Use the signature block approved by the IRB. Complete all items in the signature block, including dates and applicable checklists.

The following are the requirements for long form consent documents:

- The participant or representative signs and dates the consent document.
- The individual obtaining consent signs and dates the consent document.
- Whenever the IRB or the sponsor require a witness to the oral presentation, the witness signs and dates the consent document.
- For participants who cannot read, and whenever required by the IRB or the sponsor, a witness to the oral presentation signs and dates the consent document.
- A copy of the signed and dated consent document is to be provided to the participant.

The following are the requirements for short form consent documents:

- The participant or representative signs and dates the short form consent document.
- The individual obtaining consent signs and dates the summary.
- The witness to the oral presentation signs and dates the short form consent document and the summary.
- Copies of the signed and dated consent document and summary are provided to the person(s) signing those documents.

See [SOP: Written documentation of Consent \(HRP-091\)](#) for more information.

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How do I submit a modification?

Complete the Modification form in ETHOS and attach all requested supplements, have the PI submit the form by clicking the “Submit” activity. Investigators should upload track-change versions of modified documents that were previously approved by the IRB. Please note that research must continue to be conducted without inclusion of the modification until IRB approval is received.

Important Note: A title change is unnecessary if the correct CON number has been associated with the study in ETHOS. If a different title is requested, this will likely require a new study submission in ETHOS. See “[How will the modification be reviewed?](#)” and “[Are there circumstances that would require submission of a new IRB application?](#)”

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How will the modification be reviewed?

OHRP [states](#) that any change that materially affects the risk/benefit assessment should not be considered minor. The following are examples of the types of changes or circumstances that may require non-committee or committee review or require a new IRB application before it can be reviewed by the IRB.

Some substantive modifications require submission of a new IRB application. Please refer to “Circumstances that would require submission of a new IRB application?” section for additional information.

Changes generally reviewed in Non-Committee Review	Changes generally reviewed in Committee Review
<ul style="list-style-type: none">a. Cosmetic or editorial changes to participant facing materials or study materials (i.e. consent document, recruitment material, change in order of questionnaire items)b. Minor changes to the recruitment or consent processc. Minor changes that do not affect previous risk/benefit assessment:<ul style="list-style-type: none">a. Payment method or amountb. Statistically small change to the number of participants or volume of sample collectionsd. Change in equally qualified study personnele. Addition of a new study site (in most cases)	<ul style="list-style-type: none">(i) Change that may or will increase the risk to participants<ul style="list-style-type: none">a. Change to inclusion/exclusion criteria(ii) Elimination of a study arm or addition of a new participant population(iii) Newly identified risks to participants(iv) Change in P.I. that may not be equally qualified as prior P.I.

f. Translations of study materials already reviewed and approved by the IRB g. Adding a new procedure that is identified in one of the expedited review categories and involves no more than minimal risk	
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Are there circumstances that would require submission of a new IRB application?

Yes, it is important to consider whether the modification may warrant submission of a new application to the IRB. Examples of circumstances that will result in a request for a new IRB application are as follows:

- Two of the three P's change: Purpose, Population, Procedures (excluding anticipated changes to adaptive clinical trial designs or changes evaluated by the FDA)
- Adding new personnel to an existing protocol who plan to conduct a research study using the existing study data/specimens
- Frequent changes that cumulatively result in confusion about the study's purpose or aims
- One IRB application is required for each business and industry sponsored protocol. For example, if a business and industry study starts off with a phase I/II study plan and then proceeds with an open-label extension study, the open-label study would require a new IRB application.
- Frequent changes in personnel and funding that cumulatively result in confusion and therefore considered a risk attribute that may result in a QA Audit.
- Adding additional funding where the grant will cover new aims that expand upon the original IRB approved study.

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When do I submit a modification versus reportable new information?

There has been some confusion about when to submit a report versus when to submit a modification.

Modifications: In general, whenever you are planning to make changes, submitting a modification is the appropriate choice. This can include changes to recruitment or consent procedures or materials, survey instruments, and changes in personnel.

Report of New Information: The Report of New Information feature in ETHOS should be used whenever an event occurs within your study that meets prompt reporting requirement (see "[What should be reported promptly to the University of Minnesota IRB?](#)").

Sometimes you may need to complete both types of submissions at the same time as they are related. A good example of this is when a new risk or increased risk has been identified that prompts changes to study materials such as a consent form, protocol, or investigator's brochure. For submissions that should be reviewed in tandem, make sure to link the Report of New Information to both the main study and accompanying modification. You can also use "Add a Comment" to note that the two submissions are related.

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How do I submit continuing review?

You must submit your Continuing Review no later than 30 days prior to the last day of approval in order for your study to be reviewed and approved for another Continuing Review period. Complete the Continuing Review form in ETHOS and attach all requested supplements, and have the PI submit the form by clicking the

“Submit” activity. The continuing review form will prompt investigators to provide information regarding the progress of the study. When completing this form, you will be required to specify enrollment totals. Enrollment is defined as eligible, appropriately informed individuals agreeing to participate in a study who have signed the informed consent. For data and/or specimen only protocols, this number should reflect the total number of data and/or specimens accessed for research purposes. This number should not exceed the total number of subjects requested in the approved protocol. If you wish to request additional subjects, a modification should be submitted for review.

Before submitting the research for initial review, you must:

- Determine whether any member of the research staff has a financial interest related to the research. A “yes” or “no” answer is sufficient. There is no need to obtain additional details.
- Obtain the verbal or written agreement of each member of the research staff to his/her role in the research.
- Have ready information regarding enrollment:
 - TOTAL: Identify the total number of participants enrolled at the investigator’s site to date.
 - SINCE LAST CONTINUING REVIEW: Identify the number of new participants enrolled at the investigator’s site since the last continuing review or since the initial approval if this is the first continuing review.
 - TOTAL STUDY WIDE: Identify the number of participants enrolled in the study as a whole to date.

Note: If it is a multi-site study, the researcher will likely have to gather enrollment data from the sponsor. If this is a single-site study, this number should be the same number reported for the local site.

If the continuing review involves modifications to previously approved research, submit those modifications either as a combined Modification and Continuing Review or as a separate request for Modification using the Modification form in ETHOS.

If the continuing review application is not received by the date requested in the approval letter, you will be restricted from submitting new Human Research until the completed application has been received.

If you are submitting your Continuing Review application within 30 days of the expiration, the IRB Office discourages you from making modifications to your study at that time.

If the approval of Human Research expires because you have failed to submit the Continuing Review application or you submitted the Continuing Review application without enough time for IRB review prior to expiration, all Human Research procedures related to the protocol under review must cease, including recruitment, advertisement, screening, enrollment, consent, interventions, interactions, and collection or analysis of private identifiable information. Continuing Human Research procedures if approval has expired is a violation of university policy and IRB requirements. Investigators may be required to submit a Report of New Information (RNI) to report this as non-compliance and include corrective and preventive actions to minimize lapses in IRB approval in the future. Lapses in IRB approval must be avoided by investigators. Frequent lapses in IRB approval may result in a determination by the IRB of continuing non-compliance.

If current subjects will be harmed by stopping Human Research procedures that are available outside the Human Research context, provide these on a clinical basis as needed to protect current subjects. If current subjects will be harmed by stopping Human Research procedures that are not available outside the Human Research context, immediately contact the IRB chair and provide a written list of the currently enrolled subjects and why they will be harmed by stopping Human Research procedures.

If the IRB reviewed your Continuing Review application, but requires modifications to secure approval, you should submit those modifications in a timely fashion so they can be reviewed before your study transitions to a lapsed state in ETHOS. In cases where the IRB believes a lapse may occur, the IRB will indicate what study procedures may take place during that period. You are responsible for responding to modifications required as soon as possible for the study to transition back to an approved state.

Adverse Event Logs and Continuing Review

Effective March 27, 2017, submitting logs of events at continuing review is not required. Logs of events that occurred prior to validation of pre-ETHOS approved studies need not be submitted to the University of Minnesota IRB.

For specific directions on how to submit a Continuing Review application in ETHOS, see [How to Submit a Continuing Review in ETHOS](#).

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What should be reported promptly to the University of Minnesota IRB?

When the University of Minnesota is serving as the IRB of record for the study, reportable events and new information should be promptly reported (within five business days of learning of the event) to the IRB in ETHOS (See [How do I Submit Reportable New Information?](#)). These include, but are not limited to, Unanticipated Problems Involving Risks to Subjects or Others (UPIRTSO).

1. Unanticipated Problems Involving Risks to Subjects or Others Assessment Criteria (all must be true):
2. Is unexpected (in terms of nature, severity, or frequency) given (a) the procedures described in the research protocol documents (e.g., the IRB-approved research protocol and informed consent document) and (b) the characteristics of the human subject population being studied.
3. Is related or possibly related to participation in the research (in this Instruction, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research).
4. Suggests that the research places human subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

It is the responsibility of investigators and research staff to follow the written protocol approved by the IRB. When investigators and/or research staff do not follow the written protocol it may require reporting to the IRB if it meets one or more of the categories below:

- 1) Violations that harmed participants/subjects or others or that indicate increased risk of harm;
- 2) Deviations committed to eliminate an immediate hazard for a participant/subject; or
- 3) Researcher failure (due to the action or inaction of the investigator or research staff) to follow the protocol.

The IRB requires reporting researcher failure whether or not the deviation from the protocol affects the scientific soundness of the research plan or the rights, safety, or welfare of human subjects.

Deviations from the protocol that an investigator and research staff involved in the conduct of the research are able to identify before they occur, but cannot prevent from occurring do not require reporting to the IRB. An example is a research participant who is on a business trip and calls the investigator to announce that she is stuck in a snow storm and cannot be at a study visit scheduled for the next day. The investigator knows, in advance, that the deviation will occur but it is not under the investigator or research team's control to avoid.

Promptly reportable events include:

1. Unexpected Death: Unexpected death of a locally enrolled participant/subject who has not withdrawn from the research whether the death is considered related to the research or not. Death is considered

unexpected if the risk of death is not listed in the consent form or is not listed as a possible event in protocol-related documents such as the IRB approved protocol or the Investigator's Brochure.

2. Risk: Information that indicates a new or increased risk, or a safety issue. For example:
3. New information (e.g., an interim analysis, safety monitoring report, publication in the literature, sponsor summary report, or investigator finding) indicates an increase in the frequency or magnitude of a previously known risk, or uncovers a new risk. Do not submit Investigational New Drug (IND) safety letters, Medwatch reports, or other such individual reports to the IRB unless, in the opinion of the investigator, the event or information in the report constitutes a UPIRTSO or the report requires a change to the protocol and/or the consent form.
4. An adverse event that indicates a potential increase in risk or reduction in benefit (such as those that may prompt a change to the protocol or consent form).
5. An investigator brochure, package insert, or device labeling is revised to indicate an increase in the frequency or magnitude of a previously known risk, or to describe a new risk.
6. Withdrawal, restriction, or modification of a marketed approval of a drug, device, or biologic used in a research protocol.
7. Protocol violation that harmed subjects or others or that indicates participants/subjects or others might be at increased risk of harm.
8. Complaint of a participant/subject that indicates participants/subjects or others might be at increased risk of harm or at risk of a new harm.
9. Any changes significantly affecting the conduct of the research outside of the investigator's control or not directed by the investigator, e.g., a new therapy for the condition under study is proving highly effective.
10. Harm: Any harm experienced by a participant/subject or other individual that, in the opinion of the investigator, is unexpected and at least probably related to the research procedures.
11. A harm is "unexpected" when its specificity or severity is inconsistent with risk information previously reviewed and approved by the IRB in terms of nature, severity, frequency, and characteristics of the study population.
12. A harm is "probably related" to the research procedures if, in the opinion of the investigator, the research procedures more likely than not caused the harm.
13. Non-compliance: Allegation of investigator or study team noncompliance or finding of investigator or study team noncompliance.
14. Audit: Audit, inspection, or inquiry by a federal agency (e.g. FDA Form 483).
15. Report: Data safety monitoring reports from councils, committees, or boards charged with data and safety oversight activities; or other reports such as FDA non-approval letters.
16. Researcher error: Failure to follow the protocol due to the action or inaction of the investigator or research staff.
17. Confidentiality: Unauthorized disclosure of confidential information.
18. Protocol Deviation: Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a subject.
19. Incarceration: Incarceration of a subject in a study not approved by the IRB to involve prisoners.
20. Complaint: Unresolved subject complaint.
21. Suspension: Suspension or premature termination by the sponsor, investigator, institution or other IRB.
22. Unanticipated adverse device effect: Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

23. Disqualification / Termination: Change in qualification of any member of the study team based on state medical board, hospital medical staff action, or other disqualification by professional board or employer.
24. Information that is not listed above does not require reporting to the University of Minnesota IRB.

Investigators are required to assess whether reports from study sponsors meet prompt reporting requirements. Reports submitted by study sponsors directly to the IRB will be returned with a request to the sponsor to ensure forwarding to the local study investigator.

When an external IRB is serving as the IRB of record for the study, see [What do I submit to the University of Minnesota IRB after my study is approved for reliance on an External IRB?](#)

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How do I submit Reportable New Information?

Complete the Report New Information (RNI) form in ETHOS, making sure to provide enough details for the IRB to understand the issue being reported. If the new information is specific to a particular study, report that information from within the Study Workspace so that an association will be made automatically between the report and the study itself.

If a Reportable New Information item requires revisions to study materials (i.e. informed consent document) and this modification is still in progress, include a comment in the RNI submission. If the modification related to the RNI is ready for IRB review, submit these changes using the Modification submission process and include a comment that this modification is related to an RNI submission and include the RNI ETHOS ID Number in the comment for easy reference.

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Do I submit clinical research monitoring reports to the IRB?

Effective October 1, 2017, written reports of study monitors will require central filing with the Quality Assurance Program of the HRPP and no longer require mandatory submission to the IRB. This change is being carried out in light of the full migration of all clinical research protocols to ETHOS and aligns with planned global changes described in the Advancing Human Research Protections [Final Monitoring Report](#).

Investigators are required to submit promptly reportable events to the IRB within five business days of discovery of the event. Occasionally, such events are identified during clinical monitoring and, as such, must be reported to the IRB accordingly.

To submit monitoring reports to the Quality Assurance Program, complete this form. You'll be asked to attach the monitoring report to the form.

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What should I do if I receive a complaint or concern about my study?

You should make a good faith effort to promptly respond to – and try to resolve – any study-related complaint or concern that you receive or of which you are aware.

If the item is significant, you are also required to promptly report the complaint or concern to the IRB. See “How do I submit Reportable New Information” for instructions on prompt reporting to the IRB. An item is considered significant if any of the following are true:

- It may adversely impact a participant’s or a potential participant’s safety, rights or welfare.
- It requires a change to the study protocol or consent form.

- It remains unresolved despite a good faith effort by the researcher to resolve it.
- It involves noncompliance or an allegation of noncompliance. See [HRP-001-SOP: Definitions](#) for the definition of “noncompliance”.
- Reporting has been requested by the Quality Assurance Program related to an item submitted directly to the HRPP. See “[What happens when the HRPP receives complaints or concerns directly?](#)” for more information.

It is understood that some complaints and concerns that you receive are relatively minor (e.g., a participant complaint about a late payment that can be quickly resolved). One-time, minor complaints that can be quickly resolved generally do not require reporting to the IRB.

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What happens when the HRPP receives complaints or concerns directly?

The HRPP is concerned about the safety, rights, and welfare of all individuals participating in research at UMN and its affiliated sites. All concerns and complaints are taken seriously.

Complaints or concerns may be [submitted directly to the HRPP](#) by anyone, including research participants, family members and representatives, and study team members. The HRPP is required to respond to all concerns and complaints received.

The Quality Assurance Program will attempt to resolve minor concerns or complaints with the complainant, if appropriate. This may include referring the participant to the study team.

If the item is judged to be significant, or if it cannot be resolved easily, additional actions will be taken. This often includes requesting that the researcher report the item to the IRB as Reportable New Information.

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Do I need to inform participants if significant new findings are developed during the course of my research?

Consent is an ongoing process and investigators should engage participants in consent discussions throughout the study. Investigators should also be aware that federal regulations at 45 CFR 46.116 (b)(5) and 21 CFR 50.25 (b)(5) state that, when appropriate, the informed consent document include a statement that “significant new findings developed during the course of the research which may relate to the participant’s willingness to continue participation will be provided to the participant.” This is particularly true when a substantive change has been made to the study protocol/consent such as:

1. new findings that change the risk/benefit profile including the identification of new risks, an increase in the magnitude of known or suspected risks, or a decrease in the expected benefit;
2. study procedures have been added, modified, or removed; or
3. new alternative treatments become available

Although there may be various methods by which to provide new information to participants, the most common approach is to prepare a revised consent form and ask participants to re-consent to the research. Investigators must notify the IRB promptly of significant new findings and they are encouraged to describe plans for re-consent of participants.

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What if my Human Research is suspended or terminated?

If the IRB suspends or terminates your Human Research, the IRB will provide a statement of the reasons for suspension or termination.

- For suspension, the IRB will indicate whether some or all of the Human Research has been suspended. If, for example, the suspension applies only to the enrollment of new participants, the IRB will indicate as such.
- For termination, you must immediately cease all research activities and work with the IRB to develop a plan for safely removing participants from the research.
- If you disagree with the IRB's decision to suspend or terminate your Human Research, you may request reconsideration of that decision in the same way as you would any other IRB's decision to disapprove a submission. See the [What if I disagree with the IRB's decision?](#) section above.

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What reporting obligations does the IRB have?

HHS regulations at 45 CFR 46.103(a) and (b)(5) and FDA regulations at 21 CFR 56.108(b) require that institutions have written procedures to ensure that the following determinations are promptly reported:

- Any unanticipated problems involving risks to subjects or others (UPIRTSO);
- Any serious or continuing noncompliance with FDA or OHRP regulations or the requirements or determinations of the IRB; and
- Any suspension or termination of IRB approval.

The investigator is notified of these determinations in writing. In addition, the following officials and entities are notified: Department Head, Dean, Institutional Officials, HRPP Quality Assurance Program, and, when applicable, research partners (e.g. Fairview Research Administration or Gillette).

When reporting to regulatory entities (e.g. FDA and/or OHRP) is required, the IRB will make every effort to notify the investigator in writing, by phone, or in person prior to forwarding the report to the regulatory entity.

See "[SOP: Post Review \(HRP-052\)](#)" for information regarding the IRB's obligations to report information to regulatory and university officials and department leadership. In addition, see "[Template: External Report \(HRP-520\)](#)" for information regarding template language to be included in the external report to the regulatory entity.

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What if I need access to IRB records or rosters?

Investigators are responsible for maintaining complete study files. All IRB related study documents are located in ETHOS. Historical studies (non-ETHOS) if needed, can be requested. Information from the IRB Roster, HRP-601, is available upon request.

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What if I need institutional certification for NIH Genomic Data Sharing?

To request institutional certification for NIH Genomic Data Sharing (NIH GDS), submit a Modification for the study in ETHOS. When submitting this modification request, select "Other parts of the study." Include the request in the Modification Summary and submit any documentation in the Supporting Documents section.

For additional information on this process see:

- [“SOP: NIH GDS Institutional Certification \(HRP-064\)”](#)
- [“WORKSHEET: NIH GDS Institutional Certification \(HRP-332\)”](#)
- [“TEMPLATE LETTER: NIH GDS Institutional Certification \(HRP-528\)”](#)

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When do I closeout a study with the IRB?

A research project may be closed once the investigator has finished:

- 1) obtaining data through interaction or intervention with subjects, or obtaining identifiable private information about the subjects; and
- 2) using, studying, or analyzing identifiable private information.

Once all such activities described in the IRB-approved protocol are finished, the research project may be closed with the IRB.

For example, when the only remaining activity of a research project involves the analysis of aggregate data sets without individual subject identifiers, no further review by the IRB is necessary. At that point, the IRB can formally close the study after the investigator submits a Continuing Review to close the study to IRB oversight. Simply maintaining individually identifiable private information collected under an IRB approved protocol without using, studying, or analyzing such information is not human subjects research and does not require ongoing IRB review. Ongoing maintenance of identifiable data must conform with the actual terms of participants' consent and investigators must be aware of other rules, laws or policies that apply to the continued maintenance of identifiable data. This includes submitting a new protocol for IRB review when a new use, a new study, or a new analysis of individually identifiable private information is planned.

Identifiable private Information is defined as Private Information for which the identity of the participant is or may readily be ascertained by the investigator or associated with the information.

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How do I close out a study?

Researchers are required to submit final closeout reports when a study is permanently closed.

Complete the Continuing Review SmartForm in ETHOS and attach all requested supplements, and have the PI submit the form by clicking the “Submit” activity. See [“How to Submit Study Closure”](#) for specific instructions.

If you fail to submit a continuing review form to closeout Human Research, you may be restricted from submitting new Human Research until the completed form has been received. Failure to close a study is non-compliance with IRB requirements.

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Can I be restricted from submitting to the IRB?

Yes, under specific circumstances, investigators who are delinquent in meeting IRB requirements may be restricted from submitting additional new protocols to the IRB. All restricted investigators are notified in writing. You will be asked to immediately resolve all outstanding issues associated with IRB requirements prior to being removed from “restricted” status.

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How long do I keep or retain records?

Research regulations and policies require each investigator to retain research data not only while the research is being conducted but also after the research is completed. Retention requirements vary depending on whether federal funding was provided for the project, whether there is funding from industry with contractual provisions governing data retention, or whether the study was conducted under FDA regulations. It is recommended that researchers comply with the longest applicable standard.

It is the responsibility of the Investigator to identify and comply with the retention requirements specific to his/her research. The following are examples of potential record retention requirements that may apply to a study:

- NIH-sponsored studies must be maintained for at least 3 years after the study ends per NIH policy and for a longer time if required by regulations or local institutional policies
- Maintain signed and dated HIPAA authorizations and consent documents that include HIPAA authorizations for at least six years after completion of the research.
- For drug studies conducted under an IND, keep records for two years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until two years after the investigation is discontinued and FDA is notified.
- For device studies conducted under an IDE or abbreviated IDE, keep records for two years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol.

See also policy, [Research Data Management: Archiving, Ownership, Retention, Security, Storage, and Transfer](#), for additional information. If your Human Research is sponsored contact the sponsor before disposing of Human Research records.

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IRB Reliance Guidance: Serving as the Single IRB of Record and External IRB Review of Human Research

When is the use of a sIRB required?

Federally funded human research that is considered multi-site research or collaborative research generally requires a single IRB (sIRB). The UMN IRB will not serve as sIRB for non-federally funded research. The sIRB requirement is a federal regulatory requirement for federally funded research that is considered non-exempt human research. For more information, see “[How do I request the University of Minnesota IRB to serve as the sIRB?](#)”

See [Appendix B-5: Examples for sIRB, Reliance on an External IRB, Individual Investigator Authorization Agreements](#).

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How do I request the University of Minnesota IRB to serve as the sIRB?

The University of Minnesota evaluates requests to serve as sIRB for multi-site/collaborative human research on a case-by-case basis when UMN is the prime awardee for the grant. UMN will not agree to act as sIRB in all cases. The UMN IRB reserves the right to decline serving as the single IRB (sIRB) for any multi-

site/collaborative research where UMN will be the prime awardee for a multi-site/collaborative study required to use sIRB (see [Checklist: Criteria for UMN Serving as sIRB \(HRP-840\)](#)).”

Complete the [Single IRB Request Form](#) to initiate a request. The HRPP will use “[Checklist: Criteria for UMN Serving as sIRB \(HRP-840\)](#)” to evaluate the request and notify the UMN PI as to whether the UMN IRB will serve as sIRB, require the use of a commercial IRB or p-Site IRB as the sIRB. PIs requesting UMN IRB to serve as sIRB will be required to complete the attestation, [FORM: PI Attestation Form for UMN IRB to Serve as sIRB \(HRP-828\)](#).

Failure to submit the sIRB request prior to submitting a study in ETHOS will cause significant delays in the review process and may also result in a situation where the IRB submission will have to be withdrawn/discarded.

If the request is for a grant submission (e.g. NIH sIRB plan), contact the HRPP well in advance of the grant submission due date to ensure time to review your request and determine if the UMN IRB is willing to act as sIRB or if you will be required to utilize an external IRB as the sIRB (e.g. Advarra IRB).

In situations where UMN IRB has decided not to serve as the sIRB:

Investigators that want to appeal a decision regarding UMN serving as sIRB should submit rationale regarding the reason(s) to why UMN IRB should serve as the sIRB (e-mail appeal to relyirb@umn.edu). This appeal will be reviewed by HRPP leadership, who will make a final determination regarding the decision for UMN IRB to or not to serve as the sIRB.

For studies where UMN will have a participating site involved in an sIRB study led by a study team of another institution that will also serve as the sIRB: If the UMN PI needs a letter of support from the UMN IRB as part of a grant application, submit a request using the [Single IRB Request Form](#).

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Will the UMN IRB serve as the sIRB for SBIR/STTR Human Research?

No. The Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR), collectively the Small Business Programs, are also known as America’s Seed Fund. University of Minnesota faculty are eligible to participate in research funded by these mechanisms. However, the University of Minnesota IRB, by standard operating procedure, cannot serve as the single IRB for SBIR/STTR research. SOP: IRB Review of Conflicts of Interest (HRP-054) indicates that the UMN IRB cannot approve external study personnel that have a conflict of interest related to the research requiring IRB review and approval.

If a UMN researcher is working with a Small Business that is the recipient of the SBIR/STTR grant:

- The small business must apply for and be granted a Federal Wide Assurance AND obtain IRB approval for their role as the prime awardee of the grant (FWA Guidance)
- The University of Minnesota cannot be named or listed under the small business’ FWA.
- For any grant submitted on or after January 25, 2018 a single IRB (sIRB) of record will be used in the ethical review of non-exempt human subjects research protocols funded by the NIH that are carried out at more than one site in the United States. SBIR/STTR grants fall under this requirement.
- Beginning January 20, 2020, for federally funded research any institution located in the United States that is engaged in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States.
- The University of Minnesota IRB will review a University researcher’s request to rely on the IRB identified by the small business (see above) to meet single IRB review requirements.

It is highly recommended that University researchers contact the University of Minnesota IRB reliance staff PRIOR to grant submission.

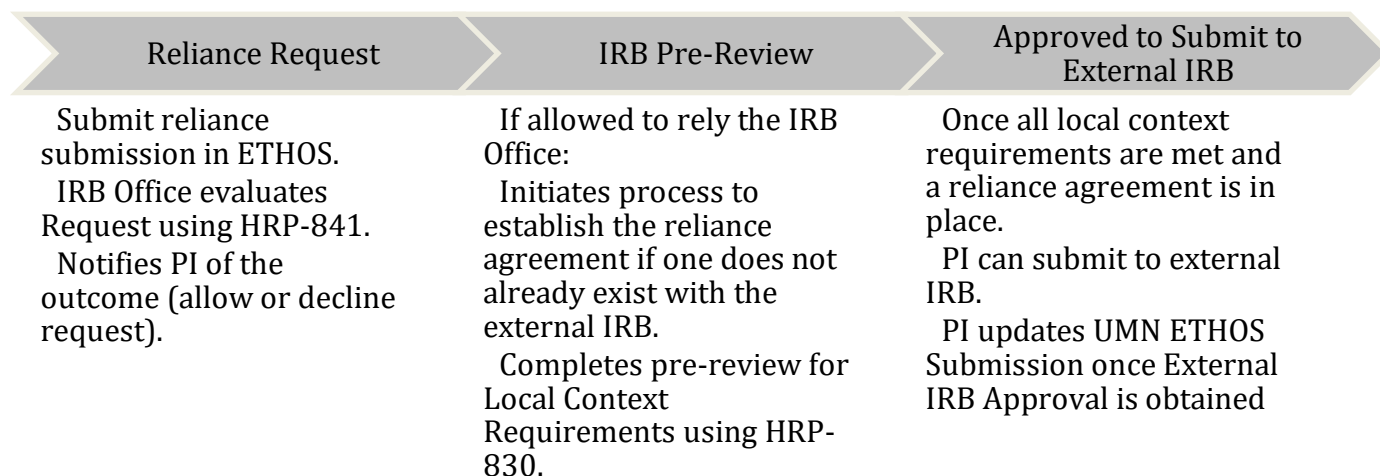
See “[How do I request reliance on an external IRB for my study?](#)” for instructions on how to request reliance in ETHOS.

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How do I request reliance on an external IRB for my study?

To request reliance on an external IRB, investigators must submit a reliance submission in ETHOS. It is highly recommended that investigators first review the criteria described in [CHECKLIST: Criteria for Relying on an External IRB \(HRP-841\)](#) prior to submitting in ETHOS. The HRPP will utilize this checklist when reviewing the request. Investigators must complete and submit the attestation, [FORM: PI Attestation Form for Reliance on an External IRB \(HRP-829\)](#).

When the UMN IRB has indicated that reliance will be allowed, the IRB staff will conduct a pre-review to ensure all local context requirements are met. Once local context requirements are met, the UMN PI will receive notification indicating that they will be able to submit to the external IRB for IRB review. The following diagram provides an overview of the reliance request process:



In situations where UMN IRB has decided not to rely on an external IRB:

Investigators that want to appeal a decision regarding reliance should submit rationale regarding the reason(s) to why UMN IRB should allow reliance on an external IRB (e-mail appeal to relyirb@umn.edu). This appeal will be reviewed by HRPP leadership, who will make a final determination regarding the decision for reliance.

See the job-aid, “[How to submit a reliance request in ETHOS](#)” for specific instructions and submission requirements.

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Does a study team using an External IRB use the U of M consent template?

If you rely on an external IRB as the IRB of record, the study sponsor or lead site will most likely provide a template consent form. You will need to revise this template consent to incorporate local University of Minnesota requirements. The University of Minnesota HRPP developed standardized language to be included (see “[WORKSHEET: Local Context Review for Relying on an External IRB \(HRP-830\)](#)”).

In some situations, the UMN IRB has agreed to other standard language as part of a Master Reliance Agreement (e.g. NCI CIRB, Advarra IRB). Investigators are responsible for adhering to those requirements, as appropriate.

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What do I submit to the University of Minnesota IRB after my study is approved for reliance on an External IRB?

Once you obtain IRB approval from the external IRB, the UMN PI must update the study in ETHOS with the following information in the STUDY submission:

- Approval Letter from the external IRB/IRB of record;
- Initial approval date by external IRB for local site; and
- Last day of approval.

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What changes must I submit to the University of Minnesota IRB after my study is approved for reliance on an External IRB?

Not all changes must be submitted to the UMN IRB. It is important to understand that even though you may not be required to submit a change to the UMN IRB, you may have ongoing obligations, such as:

- Obligations to ancillary reviewers for studies relying on an external IRB. You are responsible for working with those ancillary review groups for what may be required over the course of the study (e.g., Fairview Research Administration, Radiation Safety, CPRC, etc.).
- Requirements related to written reports of study monitors (e.g. clinical monitoring reports) for the local study site. These must also be submitted to the Quality Assurance Program Central File. To submit monitoring reports to the Quality Assurance Program (QA), complete this [form](#). You'll be asked to attach the monitoring report to the form.

The following changes or information must be submitted in ETHOS for UMN IRB review as a modification submission, as applicable, over the course of the study:

- Continuing approval from external IRB (submit as a comment, notifying the IRB Coordinator);
- Changes to study team members;
- Changes to conflict of interest status;
- Changes in funding (Note: If the grant does not cover the same research question and study procedures that have already been approved by the IRB, a new study submission in ETHOS will be required);
- Closure of the local study site;
- Prompt reporting of an unexpected death of a local research participant;
- Determination by the IRB of record of serious or continuing noncompliance, suspension, termination, or UPIRTSO for the local site; and
- Audit, inspection, or inquiry by a federal agency within five days of the investigator learning of the inspection and any written reports from federal agencies (e.g., FDA Form 483).

For instructions on submitting updates or modifications in ETHOS for reliance submissions, see the job-aid, [“How to submit an update or modification for a reliance submission.”](#)

What are my roles and responsibilities when relying on an External IRB?

Regardless of which IRB is responsible for the IRB review and oversight of your project, the University of Minnesota retains responsibility for the protection of human subjects and for compliance with applicable laws, regulations and ethical standards.

You remain responsible for compliance with all applicable federal regulations, all applicable state and local laws as well as University of Minnesota institutional requirements and policies for and relating to the research.

The Reliance Agreement for your project details the roles and responsibilities of the relying institution, including the Principal Investigator. You are responsible for following the roles and responsibilities laid out in that Agreement and any associated SOPs as well as information shared with you by the external IRB (or coordinating center) such as the external IRB policies and procedures. This includes submitting any monitoring reports to the University's Quality Assurance Program (See above for instructions).

You may not start Human Research activities until you have IRB approval from the external IRB.

IMPORTANT NOTE: You may have ongoing obligations to ancillary reviewers for studies relying on an external IRB. You are responsible for working with those ancillary review groups for what may be required over the course of the study (e.g., Fairview Research Administration, Radiation Safety, CPRC, etc.).

Also see "[FORM: PI Attestation Form for Reliance on an External IRB \(HRP-829\)](#)" for additional responsibilities. The PI will be required to sign and submit as part of the reliance submission.

What is the difference between a research site and a research location?

Research Site Engaged in Human Research Led by UMN PI

Generally, an institution/organization is considered a research site and engaged in the conduct of human research when the institution or organization is involved in any of the following ([Engagement Determination \(HRP-311\)](#)):

- Helps with the informed consent process
- Interacts or intervenes directly with participants as part of the research (data collection via interviews, survey administration)
- Obtains or analyzes personally-identifiable data or specimens
- Receives federal funding directly to the site for human subjects research.

In these circumstances, the institution or organization must either:

- Review the project locally - the site's investigator submits for IRB review at their home institution. This will often be required if the research is non-federally funded. This will always be required if the research is exempt,
- Rely on UMN IRB as the sIRB - this is most often appropriate when the research is federally funded and considered non-exempt. If federally funded, the institution/organization must have a Federal-Wide-Assurance.

Institutions/Organizations that are collaborating with the UMN PI are not considered "engaged in human subjects research" if they do not interact with subjects or the identified data, analyze de-identified data only, or assist with recruitment only.

Institutions/organizations collaborating with UMN researchers to conduct quality improvement projects that are deemed not human subjects research by the UMN IRB are not required to establish a reliance agreement with the UMN IRB.

Federalwide Assurance Requirements for Entities Collaborating or Participating in the Conduct of Research for which the U of M is the IRB of Record

Department of Health and Human Services regulations require any organization engaged in nonexempt human subjects research conducted or supported by DHHS to provide the Office of Human Research Protection written assurance of compliance with the 45 CFR 46 regulations. This written assurance, or Federalwide Assurance (FWA) is an agreement between an organization and the federal government that it will conduct its human subjects research in accordance with the regulatory requirements for the protection of human research subjects. It serves to assure that the research is being conducted in accordance with longstanding regulatory and ethical frameworks. The University of Minnesota will require an FWA for all organizations collaborating or participating in federally sponsored research. Instructions for applying for an FWA can be found here: <https://www.hhs.gov/ohrp/register-irbs-and-obtain-fwas/fwas/file-a-new-fwa/index.html>

Important Notes for UMN PIs:

UMN PIs leading multi-site or collaborative research are responsible for the research site selection process. The selection process includes confirming that a research site is adequately resourced and has personnel trained to conduct research activities.

Research Location

An institution or organization is considered a research location when it permits the UMN PI to utilize the space, access its information, or recruit its staff, clients, or constituents for a research study led by the UMN PI. This could include allowing the UMN PI to initiate a survey, conduct interviews, or access information. Under these kinds of circumstances, the research location does not need to have an FWA or IRB. The UMN PI is required to seek permission from the institution/organization before engaging in these activities and may be asked to provide documentation to the UMN IRB that permission has been granted.

See [Appendix B-5: Examples for sIRB, Reliance on an External IRB, Individual Investigator Authorization Agreements](#).

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Should I list an external institution in the ETHOS submission?

Every institution engaged in Human Subjects Research must receive IRB review and approval. Unless the UMN IRB has agreed to serve as sIRB, review for that site must be obtained from that external institution's IRB or an IRB the institution has agreed to rely on for IRB review. See "[WORKSHEET: Engagement Determination \(HRP-311\)](#)" for additional guidance on engagement in research.

- **If the External Site (e.g., university, hospital) is engaged in human subjects research:** Your protocol should include information regarding external sites/collaborators. Do not include external personnel as study team members in ETHOS. The external collaborator(s) from the external institution must ask their own IRB to review their involvement in the project or study. The UMN IRB may request verification of external site IRB approval during review of your protocol.
- **If the External Site (e.g., university, hospital) is not engaged in human subjects research:** If the U of M IRB does not consider external site(s) engaged in research, the study submission only needs to

include a description of that site's involvement. Do not include external personnel as study team members in ETHOS.

- If the external personnel are affiliated with an institution (e.g., university, hospital) with its own IRB, they should consult with their own IRB office to determine if any additional action is needed.

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In what cases will the University of Minnesota IRB consider serving as the IRB of record for an external study team member?

The University of Minnesota may, on a case-by-case basis, consider serving as the IRB of record for external collaborating independent investigator engaged in non-exempt U of M research. Requests must be submitted to relyirb@umn.edu and should include a detailed description of the individual's engagement in the study activities, their institutional affiliation, and a completed "[FORM: External Team Member Information Form \(HRP-216\)](#)."

The HRPP will use "[WORKSHEET: Individual Investigator Authorization Agreements \(HRP-832\)](#)" to evaluate the request. In general, this agreement is used for individual investigators external to the University of Minnesota and its affiliates where they are not affiliated with an institution that:

- Has its own IRB or designated IRB (e.g., a hospital or academic institution); and
- Has its own federalwide assurance ("FWA"); and
- Is routinely engaged in human research.

If the U of M has agreed to enter into an agreement, the HRPP will notify the UMN PI. The UMN PI will be required to upload a copy of the fully signed agreement, a completed "[FORM: External Team Member Information Form \(HRP-216\)](#)," in ETHOS under "External Team Members" as either part of the initial IRB submission (prior to IRB review) or as a modification submission.

See [Appendix B-5: Examples for sIRB, Reliance on an External IRB, Individual Investigator Authorization Agreements](#).

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Can an Individual Investigator Authorization Agreement (IIA) be allowed instead of a formal reliance agreement between the UMN IRB and the institution/organization?

In many cases, yes. The UMN IRB reviews the request for an IIA by using [WORKSHEET: Individual Investigator Authorization Agreements \(HRP-832\)](#).

An IIA is an agreement between the University of Minnesota and an individual collaborator that is not affiliated with the UMN or its affiliates (e.g. MHealth Fairview, Gillette Children's Specialty Care) where the individual is engaged in human research activities (see [WORKSHEET: Individual Investigator Authorization Agreements \(HRP-832\)](#)) and is either:

- 1) not acting as an employee of any institution with respect to his or her involvement in the research being conducted (collaborating independent investigator) OR
- 2) not affiliated with a FWA-holding institution, affiliated with an institution or organization that does not regularly engage in human research (collaborating institutional investigator).

Important Note:

Providing feedback on the design of a project or feedback on interview/survey questions does not constitute engagement in human subjects research. If the individual is not engaged in human research activities, they do not need to be added as personnel and an IIA is not warranted.

Community Based Participatory Research

The University of Minnesota is committed to fostering meaningful and respectful collaborations between investigators and the broad, diverse communities of our state. It is particularly important to establish these relationships with underserved communities, communities with limited access to participate in research, and those communities identified as experiencing negative health outcomes at greater rates than the majority population. Researchers are strongly encouraged to explore the boundaries of Community Based Participatory Research models. This approach encourages significant community input into the design and conduct of research but doesn't assume that the community has or needs to acquire all the skills required to conduct the research.

See [Community-Based Participatory Research Program \(CBPR\) \(nih.gov\)](#).

See [Appendix B-5: Examples for sIRB, Reliance on an External IRB, Individual Investigator Authorization Agreements](#).

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Additional Information & Resources

What printed materials are available to enhance understanding for research participants?

The University of Minnesota is a leading public research institution. A wide variety of research studies, from behavioral studies to experimental drug studies, take place here. Research volunteers can help researchers discover answers to questions to improve people's lives. Information for participants can be found on the [Research Participant Resources webpage](#). This includes:

1. [Research Participant Brochure \(HRP-104\)](#)
2. [Legally Authorized Representative Brochure \(HRP-105\)](#)
3. [Participant Bill of Rights \(HRP-106\)](#)

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What if I have questions about the IRB process or IRB review?

If you have any questions or concerns related to the process for submitting to the IRB, contact the IRB Office at:

200 Oak Street S.E.
Suite 350-2
Minneapolis, MN 55455
612-626-5654
irb@umn.edu

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What if I have concerns about the IRB process or IRB review?

If you have questions, concerns, complaints, allegations of undue influence, allegations or findings of non-compliance, or input regarding the Human Research Protection Program you may contact the HRPP, anonymously if desired, through the [online feedback form](#) or by phone. Information about reporting concerns is available at <https://research.umn.edu/units/hrpp/research-participants/questions-concerns>.

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Appendix A-1 Additional Requirements for DHHS-Regulated Research²

- When a subject decides to withdraw from a clinical trial, the investigator conducting the clinical trial should ask the subject to clarify whether the subject wishes to withdraw from all components of the trial or only from the primary interventional component of the trial. If the latter, research activities involving other components of the clinical trial, such as follow-up data collection activities, for which the subject previously gave consent may continue. The investigator should explain to the subject who wishes to withdraw the importance of obtaining follow-up safety data about the subject.
- Investigators are allowed to retain and analyze already collected data relating to any subject who chooses to withdraw from a research study or whose participation is terminated by an investigator without regard to the subject's consent, provided such analysis falls within the scope of the analysis described in the IRB-approved protocol. This is the case even if that data includes identifiable private information about the subject.
- For research not subject to regulation and review by FDA, investigators, in consultation with the funding agency, can choose to honor a research subject's request that the investigator destroy the subject's data or that the investigator exclude the subject's data from any analysis.
- When seeking the informed consent of subjects, investigators should explain whether already collected data about the subjects will be retained and analyzed even if the subjects choose to withdraw from the research.

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² <http://www.hhs.gov/ohrp/policy/subjectwithdrawal.html>

Appendix A-2 Additional Requirements for FDA-Regulated Research

- When a subject withdraws from a study:³
 - The data collected on the subject to the point of withdrawal remains part of the study database and may not be removed.
 - An investigator may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject would distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the subject's information.
 - If a subject withdraws from the interventional portion of the study, but agrees to continued follow-up of associated clinical outcome information as described in the previous bullet, the investigator must obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). IRB approval of informed consent documents is required.
 - If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the investigator must not access for purposes related to the study the subject's medical record or other confidential records requiring the subject's consent.
 - An investigator may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.
- For FDA-regulated research involving investigational drugs:
 - Investigators must abide by FDA restrictions on promotion of investigational drugs:⁴
 - An investigator, or any person acting on behalf of an investigator, must not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug.
 - This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution.
 - An investigator must not commercially distribute or test market an investigational new drug.
 - Follow FDA requirements for general responsibilities of investigators⁵
 - An investigator is responsible for ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; for protecting the rights, safety, and welfare of subjects under the investigator's care; and for the control of drugs under investigation.

³ <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126489.pdf>

⁴ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.7>

⁵ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.60>

- An investigator must, in accordance with the provisions of 21 CFR §50, obtain the informed consent of each human subject to whom the drug is administered, except as provided in 21 CFR §50.23 or §50.24 of this chapter.
- Additional specific responsibilities of clinical investigators are set forth in this part and in 21 CFR §50 and 21 CFR §56.
- Follow FDA requirements for control of the investigational drug⁶
 - An investigator must administer the drug only to subjects under the investigator's personal supervision or under the supervision of a sub-investigator responsible to the investigator.
 - The investigator must not supply the investigational drug to any person not authorized under this part to receive it.
- Follow FDA requirements for investigator recordkeeping and record retention⁷
 - Disposition of drug:
 - An investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects.
 - If the investigation is terminated, suspended, discontinued, or completed, the investigator must return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under 21 CFR §312.59.
 - Case histories.
 - An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation.
 - Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. The case history for each individual must document that informed consent was obtained prior to participation in the study.
 - Record retention: An investigator must retain required records for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.
- Follow FDA requirements for investigator reports⁸
 - Progress reports: The investigator must furnish all reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained.
 - Safety reports: An investigator must promptly report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug. If the adverse effect is alarming, the investigator must report the adverse effect immediately.
 - Final report: An investigator must provide the sponsor with an adequate report shortly after completion of the investigator's participation in the investigation.

⁶ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.61>

⁷ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.62>

⁸ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.64>

- Financial disclosure reports:
 - The clinical investigator must provide the sponsor with sufficient accurate financial information to allow an applicant to submit complete and accurate certification or disclosure statements as required under 21 CFR §54.
 - The clinical investigator must promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following the completion of the study.
- Follow FDA requirements for assurance of IRB review⁹
 - An investigator must assure that an IRB that complies with the requirements set forth in 21 CFR §56 will be responsible for the initial and continuing review and approval of the proposed clinical study.
 - The investigator must also assure that he or she will promptly report to the IRB all changes in the research activity and all unanticipated problems involving risk to human subjects or others, and that he or she will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.
- Follow FDA requirements for inspection of investigator's records and reports¹⁰
 - An investigator must upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee to have access to, and copy and verify any records or reports made by the investigator pursuant to 312.62.
 - The investigator is not required to divulge subject names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained.
- Follow FDA requirements for handling of controlled substances¹¹
 - If the investigational drug is subject to the Controlled Substances Act, the investigator must take adequate precautions, including storage of the investigational drug in a securely locked, substantially constructed cabinet, or other securely locked, substantially constructed enclosure, access to which is limited, to prevent theft or diversion of the substance into illegal channels of distribution.
- For FDA-regulated research involving investigational devices:
 - General responsibilities of investigators.¹²
 - An investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations, for protecting the rights, safety, and welfare of subjects under the investigator's care, and for the control of devices under investigation. An investigator also is responsible for ensuring that informed consent is obtained in accordance with 21 CFR §50.
 - Specific responsibilities of investigators¹³

⁹ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.66>

¹⁰ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.68>

¹¹ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.69>

¹² <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.100>

¹³ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.110>

- Awaiting approval: An investigator may determine whether potential subjects would be interested in participating in an investigation, but must not request the written informed consent of any subject to participate, and must not allow any subject to participate before obtaining IRB and FDA approval.
- Compliance: An investigator must conduct an investigation in accordance with the signed agreement with the sponsor, the investigational plan, and other applicable FDA regulations, and any conditions of approval imposed by an IRB or FDA.
- Supervising device use: An investigator must permit an investigational device to be used only with subjects under the investigator's supervision. An investigator must not supply an investigational device to any person not authorized to receive it.
- Financial disclosure:
 - A clinical investigator must disclose to the sponsor sufficient accurate financial information to allow the applicant to submit complete and accurate certification or disclosure statements required under 21 CFR §54.
 - The investigator must promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study.
- Disposing of device: Upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator must return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.
- Maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:¹⁴
 - All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports.
 - Records of receipt, use or disposition of a device that relate to:
 - The type and quantity of the device, the dates of its receipt, and the batch number or code mark.
 - The names of all persons who received, used, or disposed of each device.
 - Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.
 - Records of each subject's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. Such records must include:
 - Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent.
 - Documentation that informed consent was obtained prior to participation in the study.
 - All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the

¹⁴ <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.140>

- condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.
 - A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.
 - The protocol, with documents showing the dates of and reasons for each deviation from the protocol.
 - Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.
- Inspections¹⁵
 - Entry and inspection: A sponsor or an investigator who has authority to grant access must permit authorized FDA employees, at reasonable times and in a reasonable manner, to enter and inspect any establishment where devices are held (including any establishment where devices are manufactured, processed, packed, installed, used, or implanted or where records of results from use of devices are kept).
 - Records inspection: A sponsor, IRB, or investigator, or any other person acting on behalf of such a person with respect to an investigation, must permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation.
 - Records identifying subjects: An investigator must permit authorized FDA employees to inspect and copy records that identify subjects, upon notice that FDA has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the investigator to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.
- Prepare and submit the following complete, accurate, and timely reports¹⁶
 - Unanticipated adverse device effects. An investigator must submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.
 - Withdrawal of IRB approval. An investigator must report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.
 - Progress. An investigator must submit progress reports on the investigation to the sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly.
 - Deviations from the investigational plan:
 - An investigator must notify the sponsor and the reviewing IRB of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency.
 - Such notice must be given as soon as possible, but in no event later than 5 working days after the emergency occurred.
 - Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan, and if these changes or deviations

¹⁵ <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.145>

¹⁶ <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.150>

may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, FDA and IRB approval also is required.

- Informed consent. If an investigator uses a device without obtaining informed consent, the investigator must report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.
- Final report. An investigator must, within 3 months after termination or completion of the investigation or the investigator's part of the investigation, submit a final report to the sponsor and the reviewing IRB.
- Other. An investigator must, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

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Appendix A-3 Additional Requirements for Clinical Trials (ICH-GCP)

For the detailed FDA GCP Guidance, See [E6\(R2\) Good Clinical Practice: Integrated Addendum to ICH E6\(R1\) Guidance for Industry](#).

1. Investigator's Qualifications and Agreements

- The clinical trial should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practice and the applicable regulatory requirements.
- The investigator should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial, should meet all the qualifications specified by the applicable regulatory requirements, and should provide evidence of such qualifications through up-to-date curriculum vitae and/or other relevant documentation requested by the sponsor, the IRB, and/or the regulatory authorities.
- The investigator should be thoroughly familiar with the appropriate use of the investigational product, as described in the protocol, in the current Investigator's Brochure, in the product information and in other information sources provided by the sponsor.
- The investigator should be aware of, and should comply with, GCP and the applicable regulatory requirements.
- The investigator/institution should permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authorities.
- The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.

2. Adequate Resources

- The investigator should be able to demonstrate (e.g., based on retrospective data) a potential for recruiting the required number of suitable subjects within the agreed recruitment period.
- The investigator should have sufficient time to properly conduct and complete the trial within the agreed trial period.
- The investigator should have available an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely.
- The investigator should ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product, and their trial-related duties and functions.

3. Medical Care of Trial Subjects

- A qualified physician (or dentist, when appropriate), who is an investigator or a sub-investigator for the trial, should be responsible for all trial-related medical (or dental) decisions.
- During and following a subject's participation in a trial, the investigator/institution should ensure that adequate medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the trial. The investigator/institution should inform a subject when medical care is needed for intercurrent illnesses of which the investigator becomes aware.
- It is recommended that the investigator inform the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and if the subject agrees to the primary physician being informed.

- Although a subject is not obliged to give his/her reasons for withdrawing prematurely from a trial, the investigator should make a reasonable effort to ascertain the reasons, while fully respecting the subject's rights.
4. Communication with IRB
- Before initiating a trial, the investigator/institution should have written and dated approval opinion from the IRB for the trial protocol, written informed consent form, consent form updates, subject recruitment procedures (e.g., advertisements), and any other written information to be provided to subjects.
 - As part of the investigator's/institution's written application to the IRB, the investigator/institution should provide the IRB with a current copy of the Investigator's Brochure. If the Investigator's Brochure is updated during the trial, the investigator/institution should supply a copy of the updated Investigator's Brochure to the IRB.
 - During the trial the investigator/institution should provide to the IRB all documents subject to review.
5. Compliance with Protocol
- The investigator/institution should conduct the trial in compliance with the protocol agreed to by the sponsor and, if required, by the regulatory authorities and which was given approval opinion by the IRB. The investigator/institution and the sponsor should sign the protocol, or an alternative contract, to confirm agreement.
 - The investigator should not implement any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documented approval opinion from the IRB of an amendment, except where necessary to eliminate an immediate hazards to trial subjects, or when the changes involves only logistical or administrative aspects of the trial (e.g., change in monitors, change of telephone numbers).
 - The investigator, or person designated by the investigator, should document and explain any deviation from the approved protocol.
 - The investigator may implement a deviation from, or a change of, the protocol to eliminate an immediate hazard to trial subjects without prior IRB approval opinion. As soon as possible, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendments should be submitted: a) to the IRB for review and approval opinion, b) to the sponsor for agreement and, if required, c) to the regulatory authorities.
6. Investigational Product
- Responsibility for investigational product accountability at the trial site rests with the investigator/institution.
 - Where allowed/required, the investigator/institution may/should assign some or all of the investigator's/institution's duties for investigational product accountability at the trial site to an appropriate pharmacist or another appropriate individual who is under the supervision of the investigator/institution.
 - The investigator/institution and/or a pharmacist or other appropriate individual, who is designated by the investigator/institution, should maintain records of the product's delivery to the trial site, the inventory at the site, the use by each subject, and the return to the sponsor or alternative disposition of unused product. These records should include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational product and trial subjects. Investigators should maintain records that document adequately that the subjects were provided the

doses specified by the protocol and reconcile all investigational product received from the sponsor.

- The investigational product should be stored as specified by the sponsor and in accordance with applicable regulatory requirements.
- The investigator should ensure that the investigational product are used only in accordance with the approved protocol.
- The investigator, or a person designated by the investigator/institution, should explain the correct use of the investigational product to each subject and should check, at intervals appropriate for the trial, that each subject is following the instructions properly.
- Randomization Procedures and Unblinding: The investigator should follow the trial's randomization procedures, if any, and should ensure that the code is broken only in accordance with the protocol. If the trial is blinded, the investigator should promptly document and explain to the sponsor any premature unblinding (e.g., accidental unblinding, unblinding due to a serious adverse event) of the investigational product.

7. Informed Consent of Trial Subjects

- In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirements, and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki. Prior to the beginning of the trial, the investigator should have the IRB's written approval opinion of the written informed consent form and any other written information to be provided to subjects.
- The written informed consent form and any other written information to be provided to subjects should be revised whenever important new information becomes available that may be relevant to the subject's consent. Any revised written informed consent form, and written information should receive the IRB's approval opinion in advance of use. The subject or the subject's legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the trial. The communication of this information should be documented.
- Neither the investigator, nor the trial staff, should coerce or unduly influence a subject to participate or to continue to participate in a trial.
- None of the oral and written information concerning the trial, including the written informed consent form, should contain any language that causes the subject or the subject's legally acceptable representative to waive or to appear to waive any legal rights, or that releases or appears to release the investigator, the institution, the sponsor, or their agents from liability for negligence.
- The investigator, or a person designated by the investigator, should fully inform the subject or, if the subject is unable to provide informed consent, the subject's legally acceptable representative, of all pertinent aspects of the trial including the written information and the approval opinion by the IRB.
- The language used in the oral and written information about the trial, including the written informed consent form, should be as non-technical as practical and should be understandable to the subject or the subject's legally acceptable representative and the impartial witness, where applicable.
- Before informed consent may be obtained, the investigator, or a person designated by the investigator, should provide the subject or the subject's legally acceptable representative ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial should be answered to the satisfaction of the subject or the subject's legally acceptable representative.

- Prior to a subject's participation in the trial, the written informed consent form should be signed and personally dated by the subject or by the subject's legally acceptable representative, and by the person who conducted the informed consent discussion.
- If a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any other written information to be provided to subjects, is read and explained to the subject or the subject's legally acceptable representative, and after the subject or the subject's legally acceptable representative has orally consented to the subject's participation in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally acceptable representative, and that informed consent was freely given by the subject or the subject's legally acceptable representative.
- Both the informed consent discussion and the written informed consent form and any other written information to be provided to subjects should include explanations of the following:
 - i. That the trial involves research.
 - ii. The purpose of the trial.
 - iii. The trial treatments and the probability for random assignment to each treatment.
 - iv. The trial procedures to be followed, including all invasive procedures.
 - v. The subject's responsibilities.
 - vi. Those aspects of the trial that are experimental.
 - vii. The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant.
 - viii. The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this.
 - ix. The alternative procedures or courses of treatment that may be available to the subject, and their important potential benefits and risks.
 - x. The compensation and/or treatment available to the subject in the event of trial related injury.
 - xi. The anticipated prorated payment, if any, to the subject for participating in the trial.
 - xii. The anticipated expenses, if any, to the subject for participating in the trial.
 - xiii. That the subject's participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.
 - xiv. That the monitors, the auditors, the IRB, and the regulatory authorities will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject or the subject's legally acceptable representative is authorizing such access.
 - xv. That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject's identity will remain confidential.

- xvi. That the subject or the subject's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial.
- xvii. The persons to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury.
- xviii. The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated.
- xix. The expected duration of the subject's participation in the trial.
- xx. The approximate number of subjects involved in the trial.
- Prior to participation in the trial, the subject or the subject's legally acceptable representative should receive a copy of the signed and dated written informed consent form and any other written information provided to the subjects. During a subject's participation in the trial, the subject or the subject's legally acceptable representative should receive a copy of the signed and dated consent form updates and a copy of any amendments to the written information provided to subjects.
- When a clinical trial (therapeutic or non-therapeutic) includes subjects who can only be enrolled in the trial with the consent of the subject's legally acceptable representative (e.g., minors, or patients with severe dementia), the subject should be informed about the trial to the extent compatible with the subject's understanding and, if capable, the subject should sign and personally date the written informed consent.
- Except as described above, a non-therapeutic trial (i.e. a trial in which there is no anticipated direct clinical benefit to the subject), should be conducted in subjects who personally give consent and who sign and date the written informed consent form.
- Non-therapeutic trials may be conducted in subjects with consent of a legally acceptable representative provided the following conditions are fulfilled: a) The objectives of the trial cannot be met by means of a trial in subjects who can give informed consent personally. b) The foreseeable risks to the subjects are low. c) The negative impact on the subject's well-being is minimized and low. d) The trial is not prohibited by law. e) The approval opinion of the IRB is expressly sought on the inclusion of such subjects, and the written approval opinion covers this aspect. Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Subjects in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.
- In emergency situations, when prior consent of the subject is not possible, the consent of the subject's legally acceptable representative, if present, should be requested. When prior consent of the subject is not possible, and the subject's legally acceptable representative is not available, enrolment of the subject should require measures described in the protocol and/or elsewhere, with documented approval opinion by the IRB, to protect the rights, safety and well-being of the subject and to ensure compliance with applicable regulatory requirements. The subject or the subject's legally acceptable representative should be informed about the trial as soon as possible and consent to continue and other consent as appropriate should be requested.

8. Records and Reports

- The investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.
- Data reported on the CRF, that are derived from source documents, should be consistent with the source documents or the discrepancies should be explained.

- Any change or correction to a CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry (i.e. an audit trail should be maintained); this applies to both written and electronic changes or corrections. Sponsors should provide guidance to investigators and/or the investigators' designated representatives on making such corrections. Sponsors should have written procedures to assure that changes or corrections in CRFs made by sponsor's designated representatives are documented, are necessary, and are endorsed by the investigator. The investigator should retain records of the changes and corrections.
- The investigator/institution should maintain the trial documents as specified in Essential Documents for the Conduct of a Clinical Trial and as required by the applicable regulatory requirements. The investigator/institution should take measures to prevent accidental or premature destruction of these documents.
- Essential documents should be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents should be retained for a longer period however if required by the applicable regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator/institution as to when these documents no longer need to be retained.
- The financial aspects of the trial should be documented in an agreement between the sponsor and the investigator/institution.
- Upon request of the monitor, auditor, IRB, or regulatory authority, the investigator/institution should make available for direct access all requested trial-related records.

9. Progress Reports

- The investigator should submit written summaries of the trial status to the IRB annually, or more frequently, if requested by the IRB.
- The investigator should promptly provide written reports to the sponsor, the IRB and, where applicable, the institution on any changes significantly affecting the conduct of the trial, and/or increasing the risk to subjects.

10. Safety Reporting

- All serious adverse events (SAEs) should be reported immediately to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting. The immediate reports should be followed promptly by detailed, written reports. The immediate and follow-up reports should identify subjects by unique code numbers assigned to the trial subjects rather than by the subjects' names, personal identification numbers, and/or addresses. The investigator should also comply with the applicable regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authorities and the IRB.
- Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluations should be reported to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol.
- For reported deaths, the investigator should supply the sponsor and the IRB with any additional requested information (e.g., autopsy reports and terminal medical reports).
- Premature Termination or Suspension of a Trial If the trial is prematurely terminated or suspended for any reason, the investigator/institution should promptly inform the trial subjects, should assure appropriate therapy and follow-up for the subjects, and, where

required by the applicable regulatory requirements, should inform the regulatory authorities. In addition:

- i. If the investigator terminates or suspends a trial without prior agreement of the sponsor, the investigator should inform the institution where applicable, and the investigator/institution should promptly inform the sponsor and the IRB, and should provide the sponsor and the IRB a detailed written explanation of the termination or suspension.
 - ii. If the sponsor terminates or suspends a trial, the investigator should promptly inform the institution where applicable and the investigator/institution should promptly inform the IRB and provide the IRB a detailed written explanation of the termination or suspension.
 - iii. If the IRB terminates or suspends its approval opinion of a trial, the investigator should inform the institution where applicable and the investigator/institution should promptly notify the sponsor and provide the sponsor with a detailed written explanation of the termination or suspension.
11. Final Reports by Investigator: Upon completion of the trial, the investigator, where applicable, should inform the institution; the investigator/institution should provide the IRB with a summary of the trial's outcome, and the regulatory authorities with any reports required.

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Appendix A-4 Additional Requirements for Department of Defense (DOD) research

- When appropriate, research protocols must be reviewed and approved by the IRB prior to the Department of Defense approval. Consult with the Department of Defense funding component to see whether this is a requirement.
- Civilian researchers attempting to access military volunteers should seek collaboration with a military researcher familiar with service-specific requirements.
- Employees of the Department of Defense (including temporary, part-time, and intermittent appointments) may not be able to legally accept payments to participate in research and should check with their supervisor before accepting such payments. Employees of the Department of Defense cannot be paid for conducting research while on active duty.
- Service members must follow their command policies regarding the requirement to obtain command permission to participate in research involving human subjects while on-duty or off-duty.
- Components of the Department of Defense might have stricter requirements for research-related injury than the DHHS regulations.
- There may be specific educational requirements or certification required.
- When assessing whether to support or collaborate with this institution for research involving human subjects, the Department of Defense may evaluate this institution's education and training policies to ensure the personnel are qualified to perform the research.
- When research involves U.S. military personnel, policies and procedures require limitations on dual compensation:
 - Prohibit an individual from receiving pay of compensation for research during duty hours.
 - An individual may be compensated for research if the participant is involved in the research when not on duty.
 - Federal employees while on duty and non-Federal persons may be compensated for blood draws for research up to \$50 for each blood draw.
 - Non-Federal persons may be compensated for research participation other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.
- When research involves large scale genomic data (LSGD) collected on DOD-affiliated personnel, additional protections are required:
 - Additional administrative, technical, and physical safeguards to prevent disclosure of DoD-affiliated personnel's genomic data commensurate with risk (including secondary use or sharing of de-identified data or specimens)
 - Research will apply an HHS Certificate of Confidentiality
- DoD Component security review
- When conducting multi-site research, a formal agreement between organizations is required to specify the roles and responsibilities of each party.
- Other specific requirements of the Department of Defense research be found in the "Additional Requirements for Department of Defense (DOD) Research" section in the IRB's "WORKSHEET: Additional Federal Criteria (HRP-318)."

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Appendix A-5 Additional Requirements for Department of Energy (DOE) Research

See DOE Order 443.1C

1. Research that involves one or more of the following must be submitted to the appropriate IRB for human subjects research review and determination:
 - Study of humans in a systematically modified environment. These studies include but are not limited to intentional modification of the human environment:
 - i. Study of human environments that use tracer chemicals, particles or other materials to characterize airflow.
 - ii. Study in occupied homes or offices that:
 1. Manipulate the environment to achieve research aims.
 2. Test new materials.
 3. Involve collecting information on occupants' views of appliances, materials, or devices installed in their homes or their energy-saving behaviors through surveys and focus groups.
 - Use of social media data.
 - Human Terrain Mapping (HTM).
 - All exempt HSR determinations must be made by the appropriate IRB and/or IRB office.
2. Personally identifiable information collected and/or used during HSR projects must be protected in accordance with the requirements of DOE Order 206.1, Department of Energy Privacy Program, current version. The Central DOE IRBs require submission of DOE's HRP- 490-CHECKLIST-Reviewing Protocols that use Personally Identifiable Information (PII) if your research includes PII.
3. You must report the following to the DOE human subjects research Program Manager (and, when an NNSA element is involved, the NNSA HSP Program Manager) prior to initiation of any new human subjects research project, even if it meets the regulatory definition of exempt human subjects research as outlined in 10 CFR Part 745.104, involving:
 - a. An institution without an established Institutional Review Board (IRB);
 - b. A foreign country;
 - c. The potential for significant controversy (e.g., negative press or reaction from stakeholder or oversight groups);
 - d. Research subjects in a protected class (prisoners, children, individuals with impaired decision making capability, or DOE/NNSA federal or DOE/NNSA contractor employees as human subjects, who may be more vulnerable to coercion and undue influence to participate) that is outside of the reviewing IRB's typical range/scope; or
 - e. The generation or use of classified information.
4. The IRB must be notified immediately and the DOE HSP Program Manager (and, when an NNSA element is involved, the NNSA HSP Program Manager) must be notified within 48 hours and consulted regarding planned corrective actions if any of the following occur:
 - Adverse events. Notify the IRB for all adverse events and the DOE/NNSA HSP Program Manager if the IRB determines them to be significant, as defined in DOE Order 443.1C.
 - Unanticipated problems and complaints about the research.
 - Any suspension or termination of IRB approval of research
 - Any significant non-compliance with HSP Program procedures or other requirements.
 - Any finding of a suspected or confirmed data breach involving PII in printed or electronic form. Report immediately to the IRB, the DOE/NNSA HSP Program Manager(s), and

the DOE-Cyber Incident Response Capability, in accordance with the requirements of the CRD associated with DOE O 206.1.

- Serious adverse events and corrective actions taken must be reported immediately to the IRB and the DOE/NNSA HSP Program Manager(s). The time frame for “immediately” is defined as upon discovery.
-

5. Requirements for human participant protections for classified research apply to all classified research conducted or supported by the DOE and its national laboratories, including contracts, and including Human Terrain Mapping research.
6. Researchers conducting human subjects research in any other country or on citizens or other individuals residing in that country must be cognizant of country-specific human subjects research requirements and consult the IRB regarding applicability of such requirements.
7. No human subjects research conducted with DOE funding, at DOE institutions (regardless of funding source), or by DOE or DOE contractor personnel (regardless of funding source or location conducted), whether done domestically or in an international environment, including classified and proprietary research, may be initiated without both a Federalwide Assurance (FWA) or comparable assurance (e.g., Department of Defense assurance) of compliance and approval by the cognizant Institutional Review Board (IRB) in accordance with 10 CFR §745.103. Human subjects research involving multiple DOE sites (e.g., members of the research team from more than one DOE site and/or data or human subjects from more than one DOE site) must be reviewed and approved by one of the Central DOE IRBs prior to initiation, or if authorized by the DOE and/or NNSA HSP Program Manager, other appropriate IRB of record. In all cases, an IRB Authorization Agreement (IAA) or Memorandum of Understanding (MOU) must be in place between the organization(s) conducting the HSR and the organization responsible for IRB review.
8. Human subjects research that involves DOE Federal and/or contractor employees must first be reviewed and approved by the appropriate DOE IRB (the DOE site IRB or one of the Central DOE IRBs), or if deemed more fitting by the Federally assured DOE site or Headquarters, other appropriate IRB of record, in accordance with an IAA or MOU negotiated between the DOE site or Headquarters and the organization responsible for IRB review..
9. Classified and unclassified human subjects research that is funded through the Strategic Intelligence Partnership Program (SIPP) must be reviewed and approved by the Central DOE IRB-Classified.
10. If applicable, federally funded HSR must comply with the requirements of the Paperwork Reduction Act.
11. Other specific requirements of the DOE research can be found in the “Additional Requirements for Department of Energy (DOE) Research” section in the IRB’s “WORKSHEET: Additional Federal Criteria (HRP-318).”

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Appendix A-6 Additional Requirements for Department of Justice (DOJ) Research

Additional Requirements for DOJ Research conducted in the Federal Bureau of Prisons

- Implementation of Bureau programmatic or operational initiatives made through pilot projects is not considered to be research.
- The project must not involve medical experimentation, cosmetic research, or pharmaceutical testing.
- The research design must be compatible with both the operation of prison facilities and protection of human subjects.
- Investigators must observe the rules of the institution or office in which the research is conducted.
- Any investigator who is a non-employee of the Bureau of Prisoners must sign a statement in which the investigator agrees to adhere to the requirements of 28 CFR §512.
- The research must be reviewed and approved by the Bureau Research Review Board.
- Incentives cannot be offered to help persuade inmate subjects to participate. However, soft drinks and snacks to be consumed at the test setting may be offered. Reasonable accommodations such as nominal monetary recompense for time and effort may be offered to non-confined research subjects who are both: No longer in Bureau of Prisons custody. Participating in authorized research being conducted by Bureau employees or contractors.
- A non-employee of the Bureau may receive records in a form not individually identifiable when advance adequate written assurance that the record will be used solely as a statistical research or reporting record is provided to the agency.
- Except as noted in the consent statement to the subject, you must not provide research information that identifies a subject to any person without that subject's prior written consent to release the information. For example, research information identifiable to a particular individual cannot be admitted as evidence or used for any purpose in any action, suit, or other judicial, administrative, or legislative proceeding without the written consent of the individual to whom the data pertain.
- Except for computerized data records maintained at an official Department of Justice site, records that contain non-disclosable information directly traceable to a specific person may not be stored in, or introduced into, an electronic retrieval system.
- If you are conducting a study of special interest to the Office of Research and Evaluation but the study is not a joint project involving Office of Research and Evaluation, you may be asked to provide Office of Research and Evaluation with the computerized research data, not identifiable to individual subjects, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the project.
- Required elements of disclosure additionally include:
 - Identification of the investigators.
 - Anticipated uses of the results of the research.
 - A statement that participation is completely voluntary and that the subject may withdraw consent and end participation in the project at any time without penalty or prejudice (the inmate will be returned to regular assignment or activity by staff as soon as practicable).
 - A statement regarding the confidentiality of the research information and exceptions to any guarantees of confidentiality required by federal or state law. For example, an investigator may not guarantee confidentiality when the subject indicates intent to

commit future criminal conduct or harm himself or herself or someone else, or, if the subject is an inmate, indicates intent to leave the facility without authorization.

- A statement that participation in the research project will have no effect on the inmate subject's release date or parole eligibility.
- You must have academic preparation or experience in the area of study of the proposed research.
- The IRB application must include a summary statement, which includes:
 - Names and current affiliations of the investigators.
 - Title of the study.
 - Purpose of the study.
 - Location of the study.
 - Methods to be employed.
 - Anticipated results.
 - Duration of the study.
 - Number of subjects (staff or inmates) required and amount of time required from each.
 - Indication of risk or discomfort involved as a result of participation.
- The IRB application must include a comprehensive statement, which includes:
 - Review of related literature.
 - Detailed description of the research method.
 - Significance of anticipated results and their contribution to the advancement of knowledge.
 - Specific resources required from the Bureau of Prisons.
 - Description of all possible risks, discomforts, and benefits to individual subjects or a class of subjects, and a discussion of the likelihood that the risks and discomforts will actually occur.
 - Description of steps taken to minimize any risks.
 - Description of physical or administrative procedures to be followed to: Ensure the security of any individually identifiable data that are being collected for the study.
 - Destroy research records or remove individual identifiers from those records when the research has been completed.
 - Description of any anticipated effects of the research study on organizational programs and operations.
 - Relevant research materials such as vitae, endorsements, sample consent statements, questionnaires, and interview schedules.
- The IRB application must include a statement regarding assurances and certification required by federal regulations, if applicable.
- You must assume responsibility for actions of any person engaged to participate in the research project as an associate, assistant, or subcontractor.
- At least once a year, you must provide the Chief, Office of Research and Evaluation, with a report on the progress of the research.
- At least 12 working days before any report of findings is to be released, you must distribute one copy of the report to each of the following: the chairperson of the Bureau Research Review Board, the regional director, and the warden of each institution that provided data or assistance.
- You must include an abstract in the report of findings.
- In any publication of results, you must acknowledge the Bureau's participation in the research project.
- You must expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.

- Prior to submitting for publication the results of a research project conducted under this subpart, You must provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons.
- Other specific requirements of the Department of Justice (DOJ) Research Conducted within the Federal Bureau of Prisons (BOP) can be found in the “Additional Requirements for Department of Justice (DOJ) Research Conducted within the Federal Bureau of Prisons (BOP)” section in the IRB’s “WORKSHEET: Additional Federal Criteria (HRP-318).”

Additional Requirements for DOJ Research Funded by the National Institute of Justice

- The project must have a privacy certificate approved by the National Institute of Justice Human Subjects Protection Officer.
- All investigators and research staff are required to sign employee confidentiality statements, which are maintained by the responsible investigator.
- The confidentiality statement on the consent document must state that confidentiality can only be broken if the subject reports immediate harm to subjects or others.
- Under a privacy certificate, investigators and research staff do not have to report child abuse unless the subject signs another consent document to allow child abuse reporting.
- A copy of all data must be de-identified and sent to the National Archive of Criminal Justice Data, including copies of the informed consent document, data collection instruments, surveys, or other relevant research materials.
 - At least once a year, the researcher shall provide the Chief, Office of Research and Evaluation, with a report of the progress of the research.
 - At least 12 working days before any report of findings is to be released, the researcher shall distribute one copy of the report to each of the following: the chairperson of the Bureau Research Review Board, the regional director, and the warden of each institution that provided data or assistance. The researcher shall include an abstract in the report of findings.
 - In any publication of results, the researcher shall acknowledge the Bureau's participation in the research project.
 - The research shall expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.
 - Prior to submitting for publication the results of a research project conducted under this subpart, the researcher shall provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons
- Other specific requirements of the Department of Justice (DOJ) Research Funded by the National Institute of Justice can be found in the “Additional Requirements for Department of Justice (DOJ) Research” section in the IRB’s “WORKSHEET: Additional Federal Criteria (HRP-318).”

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Appendix A-7 Additional Requirements for Department of Education (ED) Research

1. Each school at which the research is conducted must provide an assurance that they comply with the Family Educational Rights and Privacy Act (FERPA) and the Protection of Pupil Rights Amendment (PPRA).
2. Provide a copy of all surveys and instructional material used in the research. Upon request parents of children¹⁷ involved in the research¹⁸ must be able to inspect these materials.
3. The school in which the research is being conducted must have policies regarding the administration of physical examinations or screenings that the school may administer to students.
4. Other specific requirements of the Department of Education (ED) Research can be found in the “Additional Requirements for Department of Education (ED) Research” section in the IRB’s “WORKSHEET: Additional Federal Criteria (HRP-318).”

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¹⁷ Children are persons enrolled in research not above the elementary or secondary education level, who have not reached the age or majority as determined under state law.

¹⁸ Research or experimentation program or project means any program or project in any research that is designed to explore or develop new or unproven teaching methods or techniques.

Appendix A-8 Additional Requirements for Environmental Protection Agency (EPA) Research

1. Research conducted, supported, or intended to be submitted to EPA is subject to Environmental Protection Agency Regulations.
2. Intentional exposure of pregnant women or children to any substance is prohibited.
3. Observational research involving pregnant women and fetuses are subject to additional DHHS requirements for research involving pregnant women (45 CFR §46 Subpart B) and additional DHHS requirements for research involving children (45 CFR §46 Subpart D.)
4. Research involving children must meet category #1 or #2.
5. Other specific requirements of the Environmental Protection Agency (EPA) Research can be found in the “Additional Requirements for Environmental Protection Agency (EPA) Research and Research Intended to be Submitted to the Environmental Protection Agency” section in the IRB’s “WORKSHEET: Additional Federal Criteria (HRP-318).”

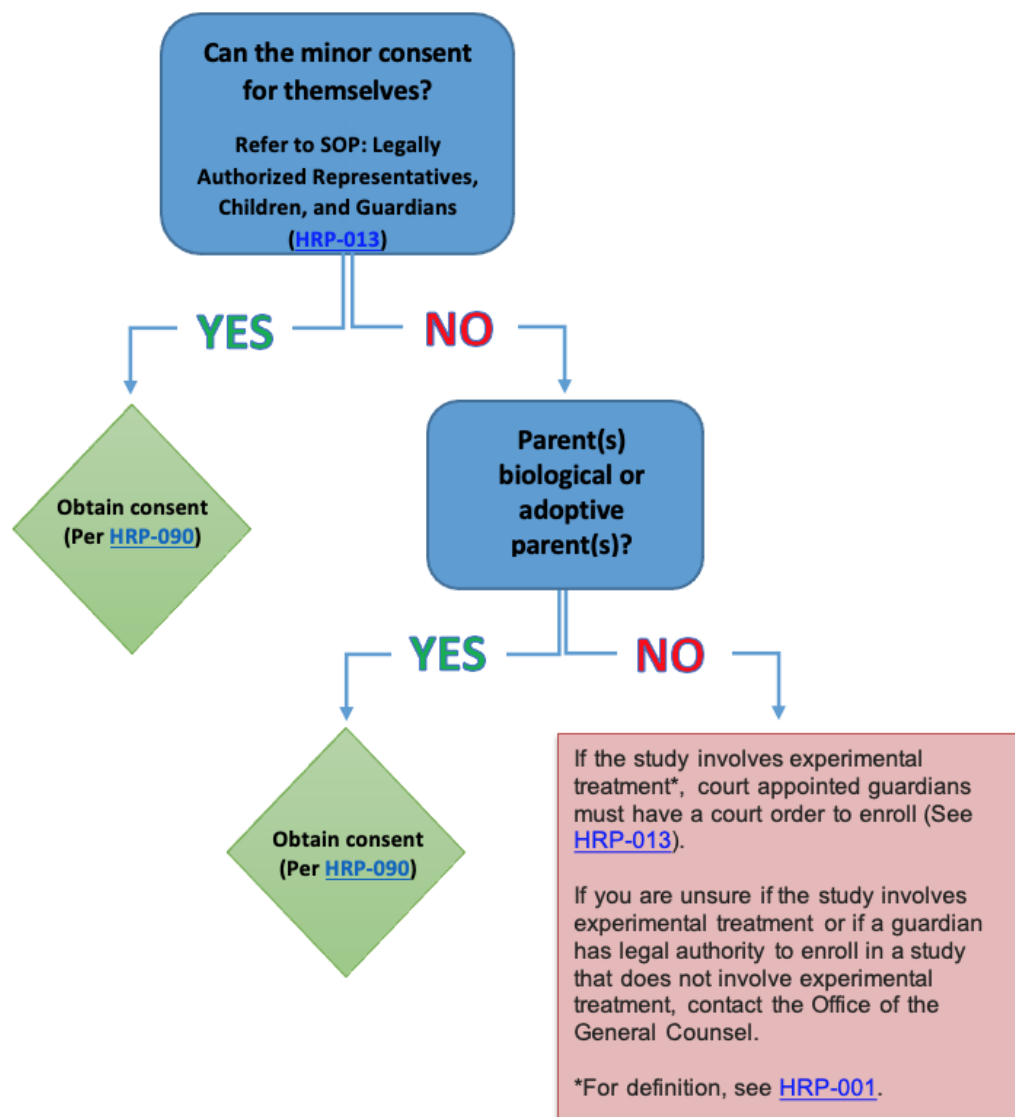
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Appendix A-9 Additional Requirements for Research Subject to EU General Data Protection Regulations (GDPR)

1. Human Research involving personal data about individuals located in (but not necessarily citizens of) European Union member states, Norway, Iceland, Liechtenstein, and Switzerland is subject to EU General Data Protection Regulations.
2. For all prospective Human Research subject to EU GDPR, contact the Office of the General Counsel (<https://ogc.umn.edu/>) to ensure that the following elements of the research are consistent with institutional policies and interpretations of EU GDPR:
 - a. Any applicable study design elements related to data security measures.
 - b. Any applicable procedures related to the rights to access, rectification, and erasure of data.
 - c. Procedures related to broad/unspecified future use consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens.
3. Where FDA or DHHS regulations apply in addition to EU GDPR regulations, ensure that procedures related to withdrawal from the research, as well as procedures for managing data and biospecimens associated with the research remain consistent with Appendices A-1 and A-2 above.
4. Where data subject to the GDPR will be processed (e.g. stored or analyzed) the contract with the processor must be reviewed by OGC and by University of Minnesota Purchasing if the contract amount is \$50,000 or above.

Appendix B-1 Research involving children diagram

The following flow diagram provides researchers guidance as to when minors may consent for themselves and when parents or guardians may consent on behalf of a child to participate in research.



Key Information

- DHHS & FDA regulations for research involving children ([Subpart D](#))
- University of Minnesota standard operating procedures, worksheets, and checklists for research involving children ([HRP-001](#), [HRP-013](#), [HRP-090](#), [HRP-091](#), [HRP-416](#))
- University of Minnesota policy ([HRP-112: Minnesota Laws Affecting Human Research](#))
- Minnesota statutes that affect research ([524.5-207](#))
- *See "Experimental Treatment" defined in [SOP: Definitions \(HRP-001\)](#)

Appendix B-2 Research involving data or specimens

The following lists data or specimen activities that may or may not require IRB review and includes IRB and HIPAA applicability and considerations. The matrix is separated into the use or collection of information or specimens.

Use of information or specimens		
Activity Description	IRB Applicability and Considerations	HIPAA Applicability
Laboratory research with commercially available tissue, cell lines or other human cells.	If the research is FDA regulated, IRB review and approval IS required.	Any Data Use Agreements (DUAs) or other agreements requested by an entity providing tissue or cells must be reviewed by the Health Information Privacy and Compliance Office .
Research with autopsy (decedent) specimens.	If the research is FDA regulated, IRB review and approval IS required.	Use of any identifiable specimens requires authorization of donor or legal representative; specimens must be secured in compliance with the HIPAA and UMN policy .
Collection of tissue from deceased donors, explanation, or plan to prior to an individual's death.	<p>Biospecimens can be collected for research from autopsies or cadaveric donors; or from tissues that were initially obtained for transplant that could not be utilized. Under the Common Rule and by FDA policy, a research participant must be living; thus obtaining biospecimens from decedents is not human subjects research.</p> <p>Some research studies involve collecting identifiable information from living research participants prior to their death and a request to collect and use tissue after death. In these cases, IRB approved consent to collect and use tissue after death is required.</p>	The HIPAA Privacy Rule must be considered because it applies to deceased individuals under certain circumstances (see HIPAA and UMN policy).

<p>The act of accessing or using patient information with the sole primary intent of improving patient care and/or clinical processes.</p>	<p>IRB approval is not required for the access or use of patient information for the sole purpose of quality improvement and assurance activities. However, investigators are encouraged to submit a Determination Form (HRP-503) to verify that the activity is not Human Research.</p> <p>See “How does quality improvement differ from research?” for more information about QA/QI activities and IRB review.</p>	<p>HIPAA Authorization is not required if the data is used only for care and clinical care purposes.</p> <p>Data must be secured in accordance with the HIPAA and UMN policy.</p>
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Use of information or specimens		
Activity Description	IRB Applicability and Considerations	HIPAA Applicability
Secondary research uses of identifiable data and/or specimens that were previously or will be collected for research	Prospective IRB approval IS required for this activity because it meets the definition of <u>Human Research</u> .	<p>HIPAA Authorization is not required if the data or specimens are de-identified per HIPAA and participants have not <u>opted-out</u> of research. De-identification cannot be done if this would circumvent the terms of original informed consent signed by the participants to which the data or specimens were collected from.</p> <p>HIPAA Authorization is not required if the data or specimens are part of a limited data set repository. However, the investigator(s) must ensure that participants have not <u>opted-out</u> of research and attest to how the data or specimens will be secured in compliance with HIPAA and UMN policy.</p> <p>Creation of a limited data set cannot be done if this would circumvent the terms of original informed consent signed by the participants to which the data or specimens were collected from.</p> <p>HIPAA Authorization IS required if the data or specimens are identifiable. The researcher can request a waiver of authorization from the IRB (see HIPAA Waiver of Authorization (HRP-441) for requirements.).</p>
	Complete and submit Data/Specimen Only Protocol Repository Protocol (HRP-5956) in ETHOS. See Waiver or Alteration of Consent Process (HRP-410) for the conditions for Waiver or Alteration of Informed Consent Relevant to Secondary Research with Identifiable Materials.	

Use of information or specimens		
Activity Description	Activity Description	Activity Description
<p>Research with previously collected <u>anonymous</u> data and/or specimens.</p> <p>Previously collected data or specimens may include left-over clinical samples, medical data, research data or research samples.</p>	<p>If the research is FDA regulated, IRB review and approval IS required.</p> <p>Investigators cannot de-identify data or specimens under his or her control for future research use without prospective IRB review and approval.</p> <p>Investigators that want to use research data or leftover research samples must also consult the original informed consent document signed by participants to ensure that subsequent use was specifically permitted.</p>	<p>If data or specimens are <u>de-identified per HIPAA</u> and the participants have not opted-out of the research, HIPAA requirements do not apply.</p>
<p>Research with previously collected <u>coded</u> data and/or specimens.</p> <p>Previously collected <u>coded</u> data or specimens may include left-over clinical samples, medical data, research data or research samples.</p>	<p>If the research is FDA regulated, IRB review and approval IS required.</p> <p>For research NOT regulated by the FDA, IRB review is not required if BOTH of the following conditions are true:</p> <ul style="list-style-type: none"> ● The data or specimens to be studied were not collected specifically for the current research; AND ● Investigator(s) cannot readily ascertain the identity of the source(s) of the coded data or specimens because one or more of the following is true: <ul style="list-style-type: none"> ● The investigator(s) and the holder of the key enter into an agreement prohibiting the release of the key to the investigator(s) under any circumstances ● IRB-approved written policies and procedures for the repository or 	<p>If data or specimens are part of a <u>limited data set</u>, investigator(s) must ensure that participants have not <u>opted-out</u> of research and attest to how the data or specimens will be secured in compliance with <u>HIPAA and UMN policy</u>.</p>

	<p>data coordinating center prohibit the release of the key to the investigator(s) under any circumstances.</p> <p>Investigators that want to use research data or leftover research samples must also consult the original informed consent document signed by participants to ensure that subsequent use was specifically permitted.</p>	
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Collection of information or specimens		
Activity Description	IRB Applicability and Considerations	HIPAA Applicability
Creation of a registry of patient information with the sole, primary intent of improving patient care and/or clinical processes.	<p>IRB approval is not required for the development of a QA/QI registry. However, investigators are encouraged to submit a Determination Form (HRP-503) to verify that the QA/QI registry is not <u>Human Research</u>.</p> <p>See “How does quality improvement differ from research?” for more information about QA/QI activities and IRB review.</p>	<p>HIPAA Authorization is not required if the data is used only for care and clinical care purposes.</p> <p>Data must be secured in accordance with HIPAA and UMN Policy.</p>
Creation of a repository that stores and distributes for future research, data and/or specimens that were previously gathered as part of clinical care and/or another research study(ies).	<p>Prospective IRB approval IS required for this activity because it meets the definition of <u>Human Research</u>.</p> <p>Complete and submit Repository Protocol (HRP-5976) in ETHOS.</p> <p>Investigators that want to add research data or leftover research samples to the repository, must also consult the original informed consent</p>	<p>HIPAA Authorization is not required if the data or specimens are <u>de-identified</u> in the repository per HIPAA and participants have not <u>opted-out</u> of research.</p> <p>HIPAA Authorization is not required if the data or specimens are part of a <u>limited data set</u> repository. However, the investigator(s) must ensure that participants have not <u>opted-out</u> of research and attest to how the</p>

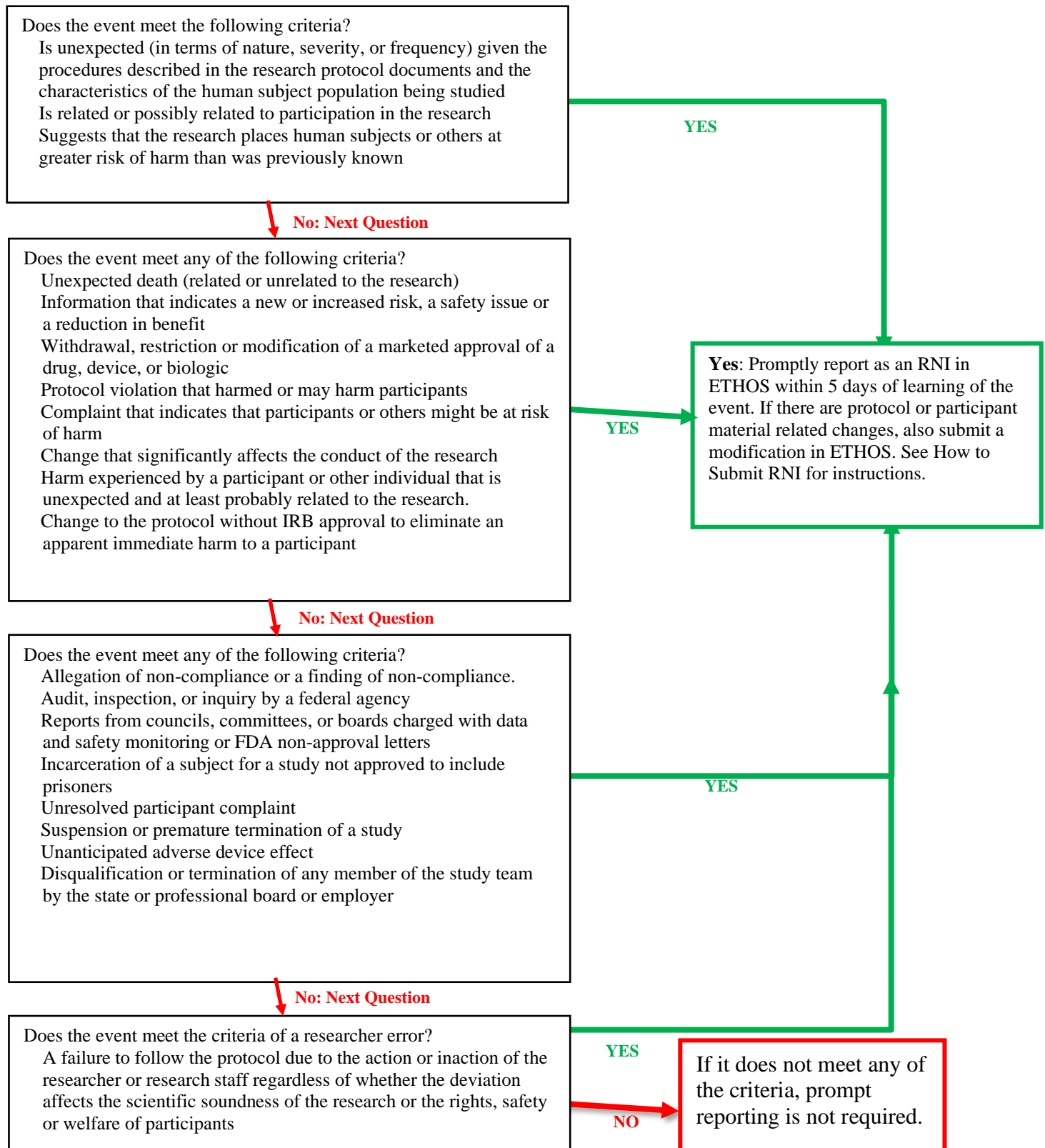
	document signed by participants to ensure that subsequent use was specifically permitted. The protocol should include a plan for obtaining informed consent when applicable (see Informed Consent Process (HRP-090) and Written Documentation of Consent (HRP-091) for requirements.	data or specimens will be secured in compliance with HIPAA and UMN policy . HIPAA Authorization IS required if the data or specimens for the repository are identifiable. The researcher can request a waiver of authorization from the IRB (see HIPAA Waiver of Authorization (HRP-441) for requirements.).
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Prospective collection of data and/or specimens for research purposes, including any additional information or specimens collected in addition to routine care activities.	<p>Prospective IRB approval IS required for this activity because it meets the definition of Human Research.</p> <p>Complete and submit Data/Specimen Only Protocol (HRP-595) in ETHOS. The protocol should include a plan for obtaining informed consent (see Informed Consent Process (HRP-090) and Written Documentation of Consent (HRP-091) for requirements.</p>	<p>HIPAA Authorization is not required if the data or specimens are de-identified per HIPAA and participants have not opted-out of research.</p> <p>HIPAA Authorization is not required if the data or specimens are part of a limited data set. However, the investigator(s) must ensure that participants have not opted-out of research and attest to how the data or specimens will be secured in compliance with HIPAA and UMN policy.</p> <p>HIPAA Authorization IS required if the data or specimens are identifiable. The researcher can request a waiver of authorization from the IRB (see HIPAA Waiver of Authorization (HRP-441) for requirements.).</p>
Collection and storage of data and/or specimens for future research uses and/or distribution.	Prospective IRB approval IS required for this activity because it meets the definition of Human Research .	HIPAA Authorization is not required if the data or specimens are de-identified per HIPAA and participants have not opted-out of research.

	<p>This is considered the development of a database, registry, or repository for research.</p> <p>Complete and submit Repository Data/Specimen Only Protocol (HRP-595) in ETHOS. The protocol should include a plan for obtaining informed consent when applicable (see Informed Consent Process (HRP-090) and Written Documentation of Consent (HRP-091) for requirements.</p>	<p>HIPAA Authorization is not required if the data or specimens are part of a limited data set. However, the investigator(s) must ensure that participants have not opted-out of research and attest to how the data or specimens will be secured in compliance with HIPAA and UMN policy.</p> <p>HIPAA Authorization IS required if the data or specimens are identifiable. The researcher can request a waiver of authorization from the IRB (see HIPAA Waiver of Authorization (HRP-441) for requirements.).</p>
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Appendix B-3 Prompt Reporting Decision Tree

The following decision tree is a tool to help the research community identify whether prompt reporting to the IRB is required. However, when in doubt, Reportable New Information should be submitted to the IRB. See “What should be reported promptly to the University of Minnesota IRB?” for more information.



Appendix B-4 Short Form and Consent Translation Requirements

The following chart was developed to help study teams understand short form and consent translation requirements. See “What about participation of individuals with limited English proficiency, meaning non-English speakers?”

Type of Study	Short Form Method Allowed?	Translated Study Consent Required?
Greater than Minimal Risk Research that plans to or will likely include non-English speaking participants.	No	Yes
Greater than Minimal Risk Research where study participation will last <u>less than 30 days</u> and will allow incidental inclusion of non-English speakers.	Yes, must receive IRB approval to use the short form method. Can only use the short form for non-English speakers of a particular language <u>three times</u> .	Possibly if the short form for non-English speakers of a particular language is used three times. If this happens, the study team must have the study consent translated into that language for the fourth non-English participant of that language. The translated consent must be submitted to the IRB as a modification for approval prior to consent.
Greater than Minimal Risk Research where study participation will last more than 30 days and will allow incidental inclusion of non-English speakers.	Yes, must receive IRB approval to use the short form method. The full-length consent form must be translated and provided to the participant within 30 days after consent via the short form method. Future consents for non-English speaking participants where a translation has already been developed cannot be consented via the short form method.	The full-length consent form must be translated and provided to the participant within 30 days after consent via the short form method.
Minimal Risk Research that plans to or will likely include non-English speaking participants.	No	Yes
Minimal Risk Research that will allow incidental inclusion of non-English speakers.	Yes	Possibly if the short form for non-English speakers of a

	<p>Can only use the short form for non-English speakers of a particular language <u>three times</u>.</p>	<p>particular language is used three times.</p> <p>If this happens, the study team must have the study consent translated into that language for the fourth non-English participant of that language.</p> <p>The translated consent must be submitted to the IRB as a modification for approval prior to consent.</p>
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Appendix B-5 Examples for sIRB, Reliance on an External IRB, Individual Investigator Authorization Agreements

The following are examples of when sIRB is required, whether the UMN IRB will serve as the sIRB, if reliance on an external IRB may be allowed, or individual investigator authorization agreements may be allowed.

Examples	sIRB Required?	UMN serve as sIRB?	IRB Authorization Agreement (Reliance Agreement) Required	Individual Investigator Authorization Agreement Possible
<p>A study is:</p> <ul style="list-style-type: none"> • federally funded (NIH, DHHS, Federal Agency) • involves US (domestic) sites • is considered non-exempt (expedited or committee review) • is considered multi-site or collaborative 	Yes	<p>Maybe.</p> <p>IRB will review requests using Checklist: Criteria for UMN IRB Serving as sIRB (HRP-840).</p>	<p>Maybe.</p> <p>If the institution or site is determined to be engaged in human subjects research (see WORKSHEET: Engagement Determination (HRP-311)).</p> <p>IRB will review the request using Checklist: Criteria for Relying on an External IRB (HRP-841).</p>	<p>Generally no.</p> <p>In most cases, external study personnel are covered under the sIRB reliance agreement.</p> <p>IRB will review the request using WORKSHEET: Individual Investigator Authorization Agreements (HRP-832).</p>
<p>A study is:</p> <ul style="list-style-type: none"> • Not federally funded (NIH, DHHS, Federal Agency) • SBIR/STTR Funded • Single site research • Exempt Research • Not human subjects research (e.g. quality improvement projects) 	No	<p>No</p> <p>As the sIRB regulatory requirement does not apply, UMN IRB will not serve as sIRB.</p>	<p>No</p> <p>UMN IRB will not serve as a Central IRB for non-federally funded research.</p> <p>Study team can request to use an external IRB as a central IRB in ETHOS (such as Advarra IRB) if one IRB review is desired.</p>	<p>Maybe.</p> <p>If external study personnel are engaged in human subjects research (see WORKSHEET: Engagement Determination (HRP-311)), UMN IRB may agree to establish an IIA.</p> <p>IRB will review the request using WORKSHEET: Individual Investigator Authorization Agreements (HRP-832).</p> <p>UMN PIs are ultimately accountable</p>

				for the conduct of external study personnel.
A school that permits investigators from another institution to conduct or distribute a research survey in the classroom; or a business that permits investigators from another institution to recruit research subjects or to draw a blood sample at the work site for research purposes. OHRP Guidance on Engagement (2008)	Not required	Not required	Not required	Not required
A clinician who provides patients with literature about a research study at another institution, including a copy of the informed consent document, and obtains permission from the patient to provide the patient's name and telephone number to investigators. OHRP Guidance on Engagement (2008)	Not required	Not required	Not required	Not Required
A research site or research site researchers are only analyzing coded, deidentified data, and no one at that site can ever access the key linking codes to identifiers.	Generally not required.	Generally not required.	No. The research site is likely not engaged in human subjects research and would likely not require a reliance agreement.	No. The researchers at the site are likely not engaged in human subjects research and would likely not require an IIA.
An individual from a non-profit organization will collaborate with a UMN PI on a community-based participatory research (CBPR) study by facilitating the focus groups. <ul style="list-style-type: none"> The UMN PI is leading the CBPR study. The UMN IRB considers the study human subjects research. The non-profit does not have an IRB and/or an FWA. 	Maybe. If the CBPR study is federally funded and considered non-exempt research. Would require that the non-profit obtain an FWA in order to	Maybe. UMN study is awarded as the prime awardee. IRB will review requests using Checklist: Criteria for UMN IRB Serving as sIRB (HRP-840) .	Maybe. Would require that the non-profit obtain an FWA in order to establish a reliance agreement or the UMN PI will have to request an IIA for federally funded research.	Maybe. The individual is engaged in human subjects research (see WORKSHEET: Engagement Determination (HRP-311)) and UMN IRB may agree to establish an IIA. IRB will review the request using WORKSHEET:

<ul style="list-style-type: none"> Focus groups will be held at the non-profit location. 	<p>establish a reliance agreement or the UMN PI will have to request an IIA for federally funded research.</p>			<p>Individual Investigator Authorization Agreements (HRP-832).</p> <p>UMN PIs are ultimately accountable for the conduct of external study personnel.</p>
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