***Institutional Review Board Submissions***

1. **PURPOSE**

This Standard Practice Guideline (SPG) describes the procedures, processes, and responsibilities for the completion and review of documentation to be submitted to the Institutional Review Board (IRB) for clinical trials.

(**MANDATORY LANGUAGE**)

1. **SCOPE**

This Standard Practice Guideline (SPG) applies to all research staff, including the Principal Investigator (PI), Co-Investigator(s) (Co-I), Study Coordinator(s), and other research professionals that may be involved in the IRB submission process.

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*[Optional: Insert any additional details necessary to further define the scope of this SPG.]*

1. **POLICY**

**Good Clinical Practices (ICH GCP)**

This Standard Practice Guideline (SPG) aligns with the Good Clinical Practice (ICH GCP) guidelines established by the International Council on Harmonization (ICH), Section 3.3.3: *The IRB should conduct initial and continuing review of trials.; 3.3.4: Determining the frequency of continuing review, as appropriate; and Section 3.1.4: The IRB should conduct continuing review of each ongoing trial at intervals appropriate to the degree of risk to human subjects, but at least once per year.* If you need the IRBMED to review a clinical trial utilizing ICH GCP this must be explicitly requested in your IRB application.

Furthermore, (ICH GCP) 4.10.2 (Progress Reports) indicates *the investigator should promptly provide written reports to the sponsor, the IEB/IEC and, where applicable, the institution on any changes significantly affecting the conduct of the trial, and/or increasing the risk to subjects.*

**FDA Regulation(s)** (if applicable)

Per 21 CFR 56.103(a) …*any clinical investigation which must meet the requirements for prior submission (as required in parts 312, 812, and 813) to the Food and Drug Administration shall not be initiated unless that investigation has been reviewed and approved by, and remains subject to continuing review by, an IRB meeting the requirements of this part.*

**University of Michigan Medical School Institutional Review Board (IRBMED)**

Investigators and research staff are responsible for reporting information concerning the approved research to the IRB in a timely fashion, understanding and adhering to the reporting guidance provided by the IRB, and not implementing any changes to the research prior to IRB approval of the change via an amendment application. This includes all information with the potential to impact the risk or benefit assessments of the research.

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**Additional Regulations or Policies** [ ]  **N/A**

*[Optional: Insert any additional project, department, sponsor, institution, state, or federal policies that apply]*

1. **DEFINITIONS**

ADVERSE EVENT (AE): Any experience or abnormal finding that has taken place during the course of a research project and was harmful to the subject participating in the research, or increased the risks of harm from the research, or had an unfavorable impact on the risk/benefit ratio. The event may or may not be caused by an intervention (e.g., headache following spinal tap, death from the underlying disease, car collision). Adverse Events also include psychological, social, emotional, and financial harms.

ASSENT: Agreement to participate in proposed research, given by an individual not competent to give legally valid informed consent (e.g., a child or mentally limited person).

* Assent means a child's affirmative agreement (verbal or written) to participate in a clinical investigation. Children age 10 and up are generally able to provide their assent.
* Assent is an adult's affirmative agreement (verbal or written) to participate in a clinical investigation. Adults may be assented (instead of consent) if they have a cognitive disability rendering them unable to consent for themselves.

BIOLOGIC: A biological product subject to licensure under the Public Health Service Act is any virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, applicable to the prevention, treatment or cure of diseases or injuries to humans. Examples include, but are not limited to, bacterial and viral vaccines, human blood and plasma and their derivatives, and certain products produced by biotechnology; any therapeutic serum, toxin, antitoxin, or analogous microbial product applicable to the prevention, treatment, or cure of diseases or injuries. (IRB definition)

CENTRAL INSTITUTIONAL REVIEW BOARD (CIRB): A single IRB that provides regulatory and ethical review services for multiple sites participating in a research study.

CONTINUING REVIEW: An IRB shall conduct continuing review at intervals appropriate to the degree of risk, but not less than once per year. Continuing review must be substantive and meaningful. Review by the convened IRB, with recorded vote, is required unless the research is otherwise appropriate for expedited review under Section 46.110. Also known as a Scheduled Continuing Review (SCR). However, under the common rule as of 1/19/2018 new research projects that qualify may not need to have annual reviews. Please see the UM IRB U-Mic regarding this @ [res\_irbmed\_continuing-changes.pptx (live.com)](https://view.officeapps.live.com/op/view.aspx?src=https%3A%2F%2Fresearch.medicine.umich.edu%2Fsites%2Fdefault%2Ffiles%2Fresource-download%2Fres_irbmed_continuing-changes.pptx&wdOrigin=BROWSELINK) or the common rule [2017-01058.pdf (govinfo.gov)](https://www.govinfo.gov/content/pkg/FR-2017-01-19/pdf/2017-01058.pdf)

(DHHS Regulations, 45 CFR 46)

eResearch Regulatory Management (eRRM): eRRM is the web-based system that centralizes the review and approval process for Human Subjects Research Applications and IBC Biosafety Registrations.

INFORMED CONSENT (IC):A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject’s decision to participate. Informed consent is documented by means of a written, signed, and dated informed consent form.

INTERNATIONAL COUNCIL ON HARMONISATION (ICH): A joint initiative involving both regulators and research-based industry representatives of the European Union, Japan, and the USA in scientific and technical discussions of the testing procedures required to assess and ensure the safety, quality, and efficacy of medicines.

INVESTIGATOR’S BROCHURE (IB): The Investigator's Brochure is a compilation of the clinical and nonclinical data on the investigational product(s) that are relevant to the study of the product(s) in human subjects. Its purpose is to provide the investigators and others involved in the trial with the information to facilitate their understanding of the rationale for, and their compliance

with, many key features of the protocol, such as the dose, dose frequency/interval,

methods of administration, and safety monitoring procedures. (ICH-GCP R2 definition)

OTHER REPORTABLE INFORMATION OR OCCURRENCE (ORIO): Any event, not an adverse event, that occurs during a clinical research study.

**PROTOCOL AMENDMENT:** A written description of any change(s) to or formal clarification of a protocol. (ICH-GCP R2 definition)

PROTOCOL DEVIATION: Departure from the IRB approved research protocol without prior IRB approval for the variation. Deviations may result from the action of the subject, researcher, or research staff.

SERIOUS ADVERSE EVENT (SAE): Any adverse experience occurring at any dose or level of participation that results in any of the following outcomes: death, a life-threatening experience, hospitalization, or prolongation of existing hospitalization, a persistent or significant disability or capacity, or a congenital anomaly or birth defect.

SPONSOR: An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial.

UNANTICIPATED PROBLEM INVOLVING RISKS TO SUBJECTS OR OTHERS (UPIRSO / UaP): Often referred as an Unanticipated Problem. An unanticipated problem may be either an actual harmful or unfavorable occurrence or any development that potentially increased the likelihood of harm occurring in the future. Assessment Criteria:

1. Unanticipated Severity:  The nature, severity, or frequency of the event(s) or information was NOT expected, given descriptions in the study documents or the characteristics of the subject population being studied.
2. Related:  There is a reasonable possibility that the procedures involved in the research caused the problem.
3. Increased Risk:  The event(s) or information suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized (including physical, psychological, economic, or social harm).

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*[Optional: Insert any additional definitions for technical or special terms used within the Standard Practice Guideline that may not be familiar to the lay reader]*

**Note:** Some of the definitions above were obtained from the IRBMed Glossary. These definitions were current as of 01-Oct-2022 and are subject to change. Please see the [IRBMed Glossary](https://research.medicine.umich.edu/office-research/institutional-review-boards-irbmed/guidance/glossary) for the most current definitions and additional guidance.

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1. **ROLES AND RESPONSIBILITIES**

**Principal Investigator/Designee**

An individual filling the role of Principal Investigator (PI) is ultimately *responsible* for making sure the initial **IRB** application and changes occurring during a clinical trial are appropriately reviewed, recorded, and reported. The PI shall be responsible for the following activities:

* Submits the initial application (eRRM - eResearch) to the local and/or central IRB, as required
* Ensures all local and/or central IRB requirements are met for the duration of the clinical trial
* Ensures that a scheduled continuing review is submitted at least annually, or more often if the IRB requests it (central and local IRBs)
* Submits any amendments to the protocol, Investigator’s Brochure, Informed Consent/Assent, IRB application, advertising material, subject materials or other trial documents that require IRB review
* Ensures that Adverse Events (AEs)/Serious Adverse Events (SAEs) are reported to the IRB per protocol and AE reporting guidelines as specified in the IRB application
* Ensures that ORIOs (e.g. protocol deviations, safety reports, etc.) are reported to the IRB per protocol and the IRB Timetable Guidelines
* Promptly reports to the IRB any changes in research activities such as the clinical trial being closed to accrual, voluntary or mandatory holds for the clinical trial, etc.
* Follows IRB guidelines for using an emergency, one-time use test article (drug, biologic or device)
* Ensures that a termination application is submitted when appropriate
* Delegates activities to other research team members, as appropriate

*[Optional: Insert any additional details regarding the responsibilities of the Principal Investigator/Designee*]

**Study Coordinator(s)/Designee**

An individual filling this role may be responsible for the following activities:

* Creates local/central IRB submissions, including scheduled continuing reviews, amendments, ORIOs, etc.
* Manages and maintains documentation related to all IRB submissions including initial application, amendments, AEs/SAEs/UaPs, ORIOs, and other submissions

*[Optional: Insert any additional details regarding the responsibilities of the Research Coordinator/Designee*]

**Co-Investigator(s)**

An individual filling this role may be responsible for the following activities:

* Notifies the PI and applicable research team members of any AEs, SAEs, UaPs, ORIOs reported during interactions with clinical trial subjects
* Notifies the PI and applicable research team members of any other changes in professional standing that have an impact on regulatory documentation such as Conflict of Interest or Financial Disclosure statements, changes in employment status, etc.

*[Optional: Insert any additional details regarding the responsibilities of the Co (Sub)-Investigator/Designee]*

**Additional Roles and Responsibilities** [ ]  **N/A**

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*[Optional: Insert any additional role(s) and responsibilities that apply to this SPG]*

1. **PROCEDURE**

**Preparing and Submitting Initial IRB Applications**

*[Describe the process for preparing and submitting the initial applications to both the local IRB and/or CIRB]*

**Preparing and Submitting Continuing Reviews and Termination Applications**

*[Describe the process for preparing and submitting the continuing reviews and termination applications to both the local IRB and/or CIRB]*

**Preparing and Submitting Amendments**

*[Describe the process for preparing and submitting amendments to local IRB and/or CIRB]*

**Preparing and Submitting Non-Serious Adverse Events**

*[Describe the process for preparing and submitting non-serious AEs to the local IRB and/or CIRB. Please review the protocol and the IRBMED link below for reporting requirements*.]

**Preparing and Submitting Serious Adverse Events**

*[Describe the process for preparing and submitting SAEs to the local IRB and/or CIRB. It should also include use of the MedWatch form in the case of an SAE in a FDA-regulated clinical trial.]*

**Preparing and Submitting Unanticipated Problems**

*[Describe the process for preparing and submitting UaPs to the local IRB and/or CIRB. This may include the preparation and submission of annual and/or progress reports*. *Please see the IRBMED link below for reporting requirements.]*

**Preparing and Submitting ORIOs**

*[Describe the process for preparing and submitting ORIOS to the local IRB and/or CIRB]*

**Tracking IRB Submissions**

[*Describe the tools used for tracking local IRB and/or CIRB submissions and due dates]*

**Additional Procedures** [ ]  **N/A**

*[Optional: Insert any additional relevant procedures. Provide enough detail to ensure the procedure is consistently carried out, without providing so much detail that violations occur due to normal or expected variations in the work.]*

1. **REFERENCES**

FDA Title 21 CFR 56.103 - Circumstances in which IRB review is required:

<http://www.ecfr.gov/cgi-bin/text-idx?SID=d888e0a5daca47d2ecced209544cdebc&mc=true&node=se21.1.56_1103&rgn=div8>

FDA Title 21 CFR 56.104 - Exemptions from IRB requirement

<http://www.ecfr.gov/cgi-bin/retrieveECFR?gp=1&SID=5b79c575275c2aa91f15b79964501546&ty=HTML&h=L&mc=true&r=SECTION&n=se21.1.56_1104>

FDA Title 21 CFR 56.108 - IRB Functions and operations

<http://www.ecfr.gov/cgi-bin/retrieveECFR?gp=1&SID=5b79c575275c2aa91f15b79964501546&ty=HTML&h=L&mc=true&r=SECTION&n=se21.1.56_1108>

International Council on Harmonisation:

<http://www.ich.org/>

<https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf>

University of Michigan IRBMED - Central IRB Information:

[Single IRB (sIRB) and Cooperative Multi-Site Research | Research A to Z (umich.edu)](https://az.research.umich.edu/medschool/guidance/single-irb-sirb-and-cooperative-multi-site-research)

University of Michigan IRBMED - Standard Operating Procedures:

<https://research.medicine.umich.edu/office-research/institutional-review-boards-irbmed/guidance/standard-operating-procedures>

University of Michigan IRBMED - Adverse Events (AEs), Other Reportable Information and Occurrences (ORIOs), and Other Required Reporting:

<https://research.medicine.umich.edu/office-research/institutional-review-boards-irbmed/guidance/adverse-events-aes-other-reportable-information-and-occurrences-orios-and-other-required-reporting>

University of Michigan IRBMED - External Adverse Event (AE) Reporting:

<https://research.medicine.umich.edu/office-research/institutional-review-boards-irbmed/guidance/adverse-events-aes-other-reportable-information-and-occurrences-orios-and-other-required-reporting/adverse-event-reporting/external-adverse-event-ae-reporting>

University of Michigan IRBMED - Other Reportable Information or Occurrence (ORIO):

<https://research.medicine.umich.edu/office-research/institutional-review-boards-irbmed/guidance/adverse-events-aes-other-reportable-information-and-occurrences-orios-and-other-required-reporting/other-reportable-information-or-occurrence-orio>

University of Michigan IRBMED - [**Standard Adverse Event Reporting Guidelines for INTERNAL AEs Occurring at UM**](http://medicine.umich.edu/medschool/sites/medicine.umich.edu.medschool/files/Adverse%20Event%20Reporting%20Guidelines%20for%20INTERNAL%20AEs%20Occurring%20at%20UM_4012015%20INWARD%20facing_0.pdf):

<https://az.research.umich.edu/sites/default/files/Adverse%20Event%20Reporting%20Guidelines%20for%20INTERNAL%20AEs%20Occurring%20at%20UM_1152018%20OUTWARD%20facing.pdf>

**(MANDATORY LANGUAGE)**

*[Optional: Insert any additional SPG references]*

1. **APPENDICES**

*[Optional: Insert any additional SPG appendices]*