***Internal Quality Assurance Process***

1. **PURPOSE**

To provide assurance that a) clinical trials utilize ethical principles that protect the rights, safety, and welfare of its participants; b) clinical trials follow governing regulations and conditions of approval imposed by the reviewing IRB or FDA; c) clinical trials follow trial management methods and procedures that are appropriate for the research and are performed in accordance with related SOPs, protocols, work instructions or other process documentation; and d) data collection and reporting is accurate, consistent, and credible.

**(MANDATORY LANGUAGE)**

1. **SCOPE**

This Standard Operating Procedure (SOP) applies to all clinical research staff, including the Principal Investigator (PI), Co-Investigator(s) (Co-I), Study Coordinator(s), and other research staff that may be involved in the Quality Assurance (QA)/Quality Control (QC) processes for clinical trials. Quality assurance and quality control procedures performed by Non-University of Michigan personnel are not within the scope of this SOP.

(**MANDATORY LANGUAGE**)

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

1. **POLICY**

This Standard Operating Procedure supports federal human subjects regulations.

The U.S. Department of Health and Human Services (HHS) human subject protections regulations at 45 CFR 46.103.(b)(4)(iii) states:

Each institution engaged in research that is federally conducted or supported shall ensure *prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.*

FDA Regulation ☐ N/A

*[If this SOP is not intended for FDA regulated clinical trials, check the N/A box]*

**Investigators:**

Investigators are responsible for protecting the rights, safety, and welfare of subjects under their care during a clinical trial. The Investigator of the clinical trial should abide by the following 21CFR regulations:

21CFR part 312.60 (IND) General Responsibilities of Investigators

*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.*

21CRF part 812.100 (IDE) General responsibilities of Investigators

*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 part 50 of this chapter.*

**Additional Policies for Sponsor Investigators:**

The University of Michigan Sponsor Investigator should abide by the following regulations and guidance documents:

21CFR part 312.50General responsibilities of sponsors

*Sponsors are responsible for selecting qualified investigators, providing them with the information they need to conduct an investigation properly, ensuring proper monitoring of the investigation(s), ensuring that the investigation(s) is conducted in accordance with the general investigational plan and protocols contained in the IND, maintaining an effective IND with respect to the investigations, and ensuring that FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug.*

21CRF part 812.40General responsibilities of Investigators

*Sponsors are responsible for selecting qualified investigators and providing them with the information they need to conduct the investigation properly, ensuring proper monitoring of the investigation, ensuring that IRB review and approval are obtained, submitting an IDE application to FDA, and ensuring that any reviewing IRB and FDA are promptly informed of significant new information about an investigation.*

ICH E-6 Section 5.1.1*: The sponsor is responsible for implementing and maintaining quality assurance and quality control systems with written SOPs to ensure that trials are conducted and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirement(s).*

In addition, ICH E-6 Section 5.1.3 states *Quality control should be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly.*

**(MANDATORY LANGUAGE)**

**Additional Regulations or Policies ☐ N/A**

**(MANDATORY LANGUAGE)**

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

1. **DEFINITIONS**

CASE REPORT FORM (CRF): A paper document or electronic questionnaire specifically used in clinical trial research. The CRF is the tool used by the sponsor of the clinical trial to collect data from each participating site. All data on each patient participating in a clinical trial are held and/or documented in the CRF, including adverse events.

CLINICAL QUALITY MANAGEMENT PLAN (CQMP): A written document, specific to the clinical research setting, which encompasses both quality assurance and quality control procedures and details the responsibility, scope, indicators measured, sample size, and frequency of these activities

DATA MANAGEMENT PLAN (DMP): A document used to outline the data management processes used, the roles and responsibilities of the individuals managing the data, and their expected deliverables

DATA AUDIT PLAN: A planning document used to verify the accuracy of the data collected and to define the degree of accuracy required in order to use the data for analysis

QUALITY ASSURANCE (QA): All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with GCP and the applicable regulatory requirement(s).

QUALITY CONTROL (QC): The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial related activities have been fulfilled.

SOURCE DATA: All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies).

SOURCE DOCUMENTS: Original documents, data, and records (e.g. hospital records, clinical and office charts, laboratory notes, memoranda, subjects’ diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photograph negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial).

SUBJECT MATTER EXPERT (SME): The individual(s) who exhibit the highest level of expertise in performing a specialized job, task, or skill within an organization

WORK INSTRUCTION (WIN): A supporting document containing detailed instructions for performing a task; a Best Practice

**(MANDATORY LANGUAGE)**

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

**Note:** Many of the definitions above were obtained from the IRBMed Glossary. These definitions were current as of 29-Sept-2015 and are subject to change. Please see the [IRBMed Glossary](http://medicine.umich.edu/medschool/research/office-research/institutional-review-boards/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 responsible for ensuring the appropriate levels of quality assurance and quality control are instituted, and that any QA or QC issues that arise are documented and addressed. These responsibilities may include but are not limited to the following:

* Identifies the appropriate QA/QC practices needed to ensure that the rights, safety, privacy and welfare of the research subjects are protected
* Identifies the appropriate QA/QC practices needed to ensure the clinical trial is conducted according to the protocol
* Identifies the appropriate QA/QC practices needed to ensure the quality and reliability of the clinical research data collected and reported
* Evaluates the frequency and rigor of QA/QC processes needed, based on the risk to research subjects, complexity of the protocol, and significance of the data
* Reviews and approves QA procedures and related guidance documents
* Ensures the designated QA/QC practices are implemented during the conduct of a clinical trial
* Reviews QA and QC findings
* Consults with statisticians and other subject matter experts to ensure the significance of QA and QC findings are appropriately interpreted and reported, as required, to the sponsor and/or reviewing IRB
* Ensures that any negative findings that surface as a result of QA or QC activities are documented and addressed
* Ensures QA and QC activities are completed prior to releasing the data for analysis
* Approves revisions to QA and/or QC processes as needed
* Selects qualified, independent internal staff to review and report on adherence to QA and QC procedures performed by the clinical research team
* Applies and fosters ethical principles during the conduct of the clinical trial

**(MANDATORY LANGUAGE)**

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

**Study Coordinator(s)/QA Staff/Designee**

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

* Assists the Investigator in determining which aspects of the clinical trial will be selected for QA/QC
* Creates QA/QC procedures and related guidance documents, i.e. Clinical Quality Management Plan (CQMP)
* Implements approved QA and QC processes
* Notifies clinical research team members of upcoming internal quality reviews, and coordinates related activities
* Consults with statisticians and other subject matter experts to ensure the significance of QA and QC findings are appropriately interpreted
* Reviews QA and QC findings; recommends corrective action when indicated
* Develops remediation plans to address frequently occurring or high risk incidents related to QA and/or QC activities
* Assesses QA and QC processes and makes recommendations for revisions as needed
* Applies ethical principles during the conduct of the clinical trial

**(MANDATORY LANGUAGE)**

*[Optional: Insert any additional details regarding the responsibilities of the Study Coordinator(s)/QA Staff/Designee]*

**Clinical Research Staff**

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

* Fulfills QA/QC responsibilities as required during the clinical trial
* Reviews QA/QC findings; takes corrective action when indicated
* Escalates concerns regarding QA or QC processes to the PI and/or QA staff
* Applies ethical principles during the conduct of the clinical trial

(**MANDATORY)**

*[Optional: Insert any additional details regarding the responsibilities of the Clinical Research Staff]*

**Internal QA/QC Reviewer(s)/Designee**

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

* Compares available process documentation to that which is required by SOPs, protocol, work instructions, and any other guidance documents associated with the conduct of a clinical trial
* Utilizes available documentation to assess compliance with relevant SOPs, protocol, work instructions, and other guidance documents
* Reports on the nature and frequency of QA and/or QC deficiencies
* Documents resolution of QA and/or QC findings
* Applies ethical principles during the conduct of the clinical trial

**(MANDATORY LANGUAGE)**

*[Optional: Insert any additional details regarding the responsibilities of the Internal QA/QC Reviewers/Designee]*

**Additional Roles and Responsibilities**  **☐ N/A**

**(MANDATORY LANGUAGE)**

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

1. **PROCEDURE**

**Protecting the Rights, Safety, Privacy, and Welfare of Participants**

*[Describe the process used to determine the nature, frequency and rigor of internal QA/QC procedures for a clinical trial based on its risk to the rights, safety, privacy, and welfare of the research participants.]*

**Administrative Procedures**

*[Describe the process used to assure that the appropriate and approved versions of clinical research documents are being utilized. (Documentation may include the protocol, informed consent/assent, telephone screen scripts, advertising, etc.)]*

*[Describe the process used to assure clinical research documents are being reviewed, approved, completed, revised, filed and stored appropriately.(Documentation includes regulatory documents, protocol, informed consent/assent, telephone screen scripts, advertising, etc.)]*

**Data Collection, Storage and Distribution**

*[Describe the process used to assure that data collection instruments such as paper and electronic Case Report Forms are being created, reviewed, approved, completed, revised, filed and stored appropriately.]*

*[Describe the process used to ensure that the data recorded on data collection instruments, such as paper and/or electronic Case Report Forms, are consistent with the source data.]*

*[Describe the process used to assure that any revisions made to the source documents, or the data recorded on data collection instruments, worksheets, etc., are documented and changed appropriately (i.e. dated, initialed; no erasing, whiteout etc.)]*

*[Describe the process used to ensure data management practices are being followed (e.g. data management plan, CRF completion guidelines, etc.)]*

*[Describe the process used to ensure that data are stored, reported, transmitted, and/or transferred in accordance with relevant regulatory, institutional, state, federal, and/or sponsor requirements]*

**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 - General Responsibilities of Investigators:

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=312.60>

FDA - Guidance for Industry E6 Good Clinical Practice - Consolidated Guidance:

<http://www.fda.gov/downloads/Drugs/guidances/ucm073122.pdf>

FDA - Office of Good Clinical Practice:

<http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/OfficeofScienceandHealthCoordination/ucm2018191.htm>

HHS.gov - U.S. Department of Health & Human Services - Human Subjects Research (45 CFR 46):

<http://www.hhs.gov/ohrp/humansubjects/guidance>

International Conference on Harmonisation (ICH):

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

National Institute of Dental and Craniofacial Research (NIDCR) - Clinical Quality Management Plan Template:

<http://www.nidcr.nih.gov/research/toolkit/Documents/Clinical_Quality_Management_Plan_Template_v2_20150413.dotx?_ga=1.31442751.1288860476.1410435240>

Society for Clinical Data Management:

<http://www.scdm.org/sitecore/content/be-bruga/scdm/About%20Us.aspx>

University of Michigan - Medical School- HIPPA:

<http://medicine.umich.edu/medschool/research/office-research/institutional-review-boards/guidance/hipaa>

University of Michigan - Operations Manual - Quality Assurance and Research Compliance:

<http://research-compliance.umich.edu/operations-manual-quality-assurance-and-research-compliance>

University of Michigan - Office of Human Research Compliance Review (OHRCR):

<http://research-compliance.umich.edu/office-human-research-compliance-review-ohrcr>

**(MANDATORY LANGUAGE)**

*[Optional: Insert any additional SOP references]*

1. **APPENDICES**

**(MANDATORY LANGUAGE)**

*[Optional: Insert any additional SOP appendices]*