OFFICE OF TRANSLATIONAL SCIENCES

Review and Conduct of Human Subject Research[1]

CONTENTS

PURPOSE

- This MAPP establishes the policies and procedures that employees in the Center for Drug Evaluation and Research (CDER) must follow when submitting human subject research for review to FDA's Institutional Review Board (IRB), the Research Involving Human Subjects Committee (RIHSC), in the Office of Science and Health Coordination (OSHC) within the Office of the Commissioner. These procedures must be followed, and written RIHSC approval or exemption obtained, before initiating any research involving human subjects. This MAPP also establishes policies and procedures pertaining to responsibilities for study conduct and oversight.

BACKGROUND

- FDA has provided assurance to the Department of Health and Human Services (HHS) that all activities related to human subject research will (1) be guided by the ethical principles outlined in the Belmont Report (see References), (2) comply with the Office for Human Research Protection's (OHRP) terms of assurance for protection of human subjects, and (3) comply with HHS regulations for the protection of human research subjects, including provisions of the Federal Policy for the Protection of Human Subjects (45 CFR part 46; 21 CFR part 50; 21 CFR part 312). As part of this assurance, FDA has established the policy that all human subject research conducted, supported, or funded in whole or in part by FDA will be reviewed and approved by an IRB established by FDA. The RIHSC is FDA's IRB. FDA has established a policy that human subject research in categories that are exempt from the regulations must be reviewed and an exemption granted in writing by the RIHSC Chair. Exempt status may not be determined by the researcher. The CDER RIHSC Liaison, appointed by and accountable to the Center Director, will review all CDER submissions before they are submitted to the RIHSC.

[1] This MAPP is a revision of an earlier MAPP originally numbered 4112.6. The MAPP's change in number reflects the establishment of the Office of Translational Sciences (OTS) within CDER.

REFERENCES

- FDA Internal Operating Procedures for FDA's Institutional Review Board, the Research Involving Human Subject Committee at http://inside.fda.gov/downloads/Document/UCM036407.pdf
- 45 CFR part 46 http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm
- "Ethical Principles and Guidelines for the Protection of Human Subjects of Research," the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, Office of the Secretary, HHS, April 18, 1979 (the Belmont Report) http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm
- "Federal-wide Assurance of Protection for Human Subjects," OHRP, HHS http://www.hhs.gov/ohrp/assurances/assurances_index.html
- Protecting Personal Health Information in Research: Understanding the HIPAA Privacy Rule (http://privacyruleandresearch.nih.gov/pr_02.asp)
- FDA Policy on the Review and Clearance of Articles to be Published in Scientific or Professional Journals (http://inside.fda.gov:9003/downloads/PolicyProcedures/GuidanceRegulations/Research/UCM009890.pdf)
- Investigator 101 Course http://first.fda.gov/detail_nf.cfm?Dir=humansubjects&File=/instructions.htm
- Investigator 101 Quiz: http://research.cber.fda.gov:591/CDER-INV101quiz/entry.htm

DEFINITIONS

- **Research Involving Human Subjects Committee (RIHSC):** FDA's Institutional Review Board (IRB), located in the Office of Science and Health Coordination, FDA.
- **Principal Investigator (PI):** The primary individual who conducts the research involving human subjects, (i.e., under whose immediate direction the research is conducted) or, in the event of an investigation conducted by a team of individuals, the responsible leader of that team.
- **Sponsor:** The FDA employee primarily responsible for FDA's role in a project involving human subjects. The FDA Sponsor is directly accountable to the RIHSC and to his or her Center Director for the conduct of FDA-sponsored human subject research.
- **Collaborator:** A participant who plays a substantive roll in the research project. This may include contributions of data or samples, participation in the design and implementation of the research plan, generation or analysis of primary data, or authorship on publications.
- **Center RIHSC Liaison:** The CDER staff member designated by the Center Director to review and assess any human subject research in which CDER employees participate, or plan to participate, before possible review by the RIHSC. The Center Liaison for CDER is:

Jan Johannessen, Ph.D.
301-796-2323
jan.johannessen@fda.hhs.gov

- **RIHSC Project Manager:** The CDER/OTS employee who has primary responsibility for managing RIHSC applications and maintaining files on all CDER protocols, investigator qualifications and training, RIHSC approvals, exemptions, and renewals. The project manager is the primary point of contact for investigators with questions regarding the RIHSC application and review process. The RIHSC Project Manager for CDER is

  Jill Coker, BSN
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- **Research:** "A systematic investigation, including research, development, testing and evaluation, designed to develop or contribute to generalizable knowledge" (45 CFR 46.102(d)).

  As described in the FDA RIHSC Internal Operating Procedures, "A key aspect of research is that there be a systematic design in advance, generally utilizing a scientific approach or protocol, for the definitive purpose of contributing to generalizable knowledge."

  Examples of activities that are not considered research include the following:

  - Creating a database of human data from existing sources (e.g., compilation of data from multiple clinical trials contained within regulatory submissions)
  - Gathering data for a compliance purpose (e.g., surveying pharmacies about what safety information is being provided with each prescription to determine whether statutory targets are being met)
  - Using Risk Minimization Action Plan (RiskMAP) or Risk Evaluation and Mitigation Strategies (REMS) data to improve patient protection
  - Compiling case reports
  - Conducting feasibility studies to determine whether sufficient data exist to conduct a research study

- **Individually Identifiable Information:** Information from which the identity of the subject is or may readily be ascertained by the investigator.

- **Human Subject Research:** Research involving "A living individual about whom an investigator . . . conducting research obtains (1) data through intervention or interaction with an individual, or (2) identifiable private information" (45 CFR 46.102(f)).

  Examples of research activities that do not constitute human subject research include the following:

  - Research using existing statistical summaries of human data (e.g., meta-analysis). Because statistical summaries of human data (e.g., from the literature or regulatory summaries) do not provide any information about individuals, this activity does not constitute human subject research.

- Research involving cell lines obtained from a vendor or other provider with whom there is a written agreement or policy that explicitly prohibits release of private information to the investigator and in which the focus of the research is the cell-type and is not related to the specific individual from whom the cells were originally derived. This does not apply to cells collected prospectively or to cells specifically collected for the proposed research.
  Please contact the RIHSC Liaison or RIHSC Project Manager to determine whether your project meets the definition of human subject research.

- **RIHSC Submission and Review Categories**

Submissions to RIHSC fall into one of three types: Initial Submission, Continuing Review (CR) Submission, or Amendment Submission.

1. **Initial Submission:** All new protocols or concepts must undergo an initial review, using one of the following review mechanisms: Concept Review, Exempt Review, Expedited Review, or Full Review, as defined below.

   - Concept Review - A concept is a short summary of proposed research to be performed by an FDA investigator or an outside researcher. Examples of concepts include Scope of Work, Request for Applications, Request for Proposals, Memorandum of Understanding, Master Agreement, Task Order, Interagency Agreements, or similar documents. Because Concepts do not involve final protocols, no research is conducted under a Concept; therefore the risk to human subjects is nonexistent. Concept submissions can therefore be reviewed by a member of RIHSC, and a signed letter of approval of the proposed concept can be issued by the RIHSC Chair within 14 working days of submission. Note that once a final contract or protocol is developed, it must be reviewed by RIHSC before work can begin.

   - Exempt Review - Under the HHS Office for Human Research Protections (OHRP) regulations, certain types of research are exempt from RIHSC review. FDA requires that research eligible for exempt status be reviewed by a member of RIHSC, and a signed letter of exemption be issued by the RIHSC Chair. This process does not involve review by the entire RIHSC. Once an exemption has been granted by the RIHSC Chair, no further review by RIHSC is required (i.e., continuing review is not needed). Exempt research performed at CDER falls into one of two categories:

     Exempt under 45 CFR 46.101(b)(2) - Research ***in adults*** involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, **unless**:

     (a) Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; **and**
     (b) Any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

     Note: This exemption does not apply to research in the pediatric population.

     Exempt under 45 CFR 46.101(b)(4) - Research involving the collection or study of existing data, documents, or pathological or diagnostic specimens if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

     See Request for Exempt Status at
     http://inside.fda.gov/ProgramsInitiatives/Drugs/ScienceResearch/UCM035467.html

- Expedited Review - The categories of research listed below may also be reviewed by the RIHSC Chair, without concurrence of the full RIHSC. An approval letter will be issued by the RIHSC Chair. As with an Exempt Review, this process does not involve review by the entire RIHSC. Approved protocols reviewed by the expedited procedure must undergo an annual review. The RIHSC may use an expedited review procedure for either or both of the following situations (see 45 CFR 46.110):

  (a) Minor changes in previously approved research during the period of 1 year (or less) for which approval is authorized

  (b) Research in which there appears to be minimal risk (defined as harm no greater than that encountered in daily life or routine physical or psychological examinations or tests)

  See Application for Expedited RIHSC Review of Research at http://inside.fda.gov/ProgramsInitiatives/Drugs/ScienceResearch/UCM035467.html.

- Full Review - Research for which a full review is required by the RIHSC includes protocols otherwise permitted under expedited review that are chosen by the RIHSC Chair for full review. Because this process involves review by the entire RIHSC, which meets only monthly, approval generally takes longer than an Expedited or Exempt review.

2. **Continuing Review (CR) Submission:** All non-exempt protocols must receive a CR annually. CR submissions may be reviewed by either
   - Expedited Review - For protocols initially reviewed using expedited procedures, for protocols with no active enrollment
   - Full RIHSC Review - For more than minimal risk protocols

   See Continuing Review Application at http://inside.fda.gov/ProgramsInitiatives/Drugs/ScienceResearch/UCM035467.html

3. **Amendment Review Submission:** All proposed changes to approved protocols must be approved before implementation using one of the following review categories:
   - Expedited Review - For changes to protocols initially reviewed using expedited procedures or for minor changes to other protocols
   - Full RIHSC Review – For any (except minor) changes to protocols involving more than minimal risk

POLICY

- All research involving human subjects, human data, or specimens from human subjects must be submitted to the RIHSC through the Center Liaison and must receive signed, written approval (including exemptions) before **any** work is permitted with these subjects, data, or specimens.
- Research that involves only aggregate data or cells lines derived from humans and that does not meet the definition of human subject research as defined above does not require RIHSC review. However, you should contact the CDER Liaison or RIHSC Project Manager to confirm this determination.
- Investigators may not self-exempt. Although a research protocol may appear to satisfy the criteria described under Exempt Review (above), research must not begin until the protocol is officially designated as "Exempt" in signed correspondence from the RIHSC Chair.
- All solicitations for work that will involve human subject research (e.g., contracts, task orders, work orders, requests for proposals) must be sent to the Center Liaison and a signed written Concept approval from RIHSC must be received before that work is announced. If the Concept is approved by

the RIHSC, the "Approval in Principle" does **not** imply or permit initiation of any research involving human subjects. Once the Concept is developed into a protocol, the protocol must be submitted to the RIHSC for review.

- Feasibility studies done under an existing contract to determine whether existing data are sufficient for a research effort do not constitute research, and therefore do not require a separate RIHSC review.
- Applications for competitive funding for research that may involve human subjects (e.g., Regulatory Science and Review Enhancement proposals) do **not** need to seek RIHSC approval before submission. Should the funding application be awarded, RIHSC approval must be obtained before initiating the project.
- If the PI is not an FDA employee (e.g., the study is an off-site contract study being conducted at a university), then the sponsor is the FDA employee accountable to RIHSC (e.g., project officer). If the PI is an FDA employee, then the FDA PI may also act as sponsor.
- The Division Director of the PI or sponsor must provide assurance that the proposed research has been reviewed for scientific merit and mission relevance, and must acknowledge managerial responsibility for oversight of the sponsor's activities related to human subject research projects.
- RIHSC has determined that "projects in which the only role of the FDA personnel is regulatory in nature, and is not the role of a clinical investigator or sponsor" do not require RIHSC review **provided** that the project involves only retrospective evaluation and analysis of human data. Some projects may encompass **both** regulatory components and those that meet criteria for classification as human subject research as defined in the regulations. If so, the research portions of the protocol must be submitted to the RIHSC and be approved or designated as "Exempt" before any work is permitted on those portions of the project. *If there is any uncertainty about requirements for a specific protocol, contact the CDER RIHSC Liaison.*

  Examples of regulatory activities for which RIHSC review is **not** required include the following:

  - Regulatory activities associated with approvals, withdrawals, labeling, guidance, and preparation of materials for advisory committee meetings
  - Primary review and retrospective analysis of human data contained within regulatory submissions (e.g., investigational new drug applications (INDs), new drug applications (NDAs), biologics license applications (BLAs))
  - Review and analysis of data, such as Adverse Event Reporting System (AERS) data, needed to perform postmarket safety monitoring activities

  Examples of activities that have a research component **or** need sufficient subject protections to require RIHSC review include the following:

  - Any clinical study or any research that involves the prospective collection of data
  - Surveys, interviews, or focus group studies
  - Research using tissues or fluids from a living human
  - Human subject research studies initially intended to serve a purely regulatory purpose, such as analysis of AERS data, but will be published as research in a peer reviewed journal.
    Note: Publishing case studies is not research, and studies involving only aggregate data do not involve human subjects.
- Any amendments to approved protocols **must** undergo RIHSC review before they can be implemented. This requirement includes studies conducted at other institutions (e.g., written

approvals from **both** the local IRB and RIHSC must be received before implementing any changes to the protocol or informed consent procedures).

- Training in the relevant human subject protection rules and regulations is required for all CDER employees involved in human subject research.

- Professional Development Activities. Many CDER professionals spend some of their time working on protocols that involve research in human subjects, either as part of their work schedule or as an outside activity. RIHSC review and action may or may not be required. One of the following situations should apply:

  1. Outside Activity. If an FDA employee participates in studies solely as an *outside activity*, this does **not** require RIHSC review, provided:
     - The work is not done on FDA time
     - The work does not use FDA equipment and/or facilities
     - The employee does not use his or her FDA affiliation in any way
  2. Research Collaborations as Professional Development. If an FDA employee participates in a human subject research protocol at another institution during work time as professional development and has a substantive role in the protocol (e.g., co-investigator status, participation in dosing determinations for study subjects, collection of research samples, data analysis), then the FDA RIHSC must formalize an agreement with the IRB of record. FDA RIHSC will transfer to the IRB of record sole responsibility for the FDA employee's activities under the protocol. A signed letter from the RIHSC Chair, along with a copy of the RIHSC/IRB agreement, must be received by the PI before any participation of the FDA employee in such a study.
  3. Clinical Care. If an FDA employee provides routine clinical care for subjects enrolled in a protocol at an institution during that employee's professional development hours, but is not substantively involved in that protocol (e.g., does not have co-investigator status, is not making dosing decisions for study subjects, is not collecting research samples, is not participating in the data analysis, protocol design, or as a co-author of a paper), no RIHSC review or approval is necessary.
  4. Research Consulting. FDA employees may be asked to serve as consultants on research studies conducted by other institutions for which FDA plays no major role. Acting as a consultant requires RIHSC approval, and must meet restrictions detailed in section XV of the RIHSC SOPs.

- Any CDER employee who seeks to publish the results of research that meets the definition of human subject research must document compliance with RIHSC requirements by including a copy of the signed RIHSC letter of approval or exemption with the manuscript clearance form prior to publication.

- Change of Intent. Occasionally, analysis of data from a study initiated solely to support regulatory intent may yield generalizable knowledge that the investigator wishes to publish. Similarly, if, during the course of research using data or samples for which the investigator did not have access to private information, the investigator gains access to the identity of the individuals to whom the previously obtained private information or specimens pertain, then the research activity now would involve human subject research. When the intent or circumstances of a study change and it becomes human subject research under the regulatory definition (cited in the Definitions section), RIHSC review is required.

- FDA Sponsors must notify the RIHSC Liaison when a project is completed. For nonexempt protocols, a final report must be submitted through RIHSC.

RESPONSIBILITIES

Center Director

- The Center Director is directly accountable to the FDA Commissioner for all research involving human subjects sponsored, conducted, or funded by CDER.
- The Center Director must designate a Center Liaison to the RIHSC. This liaison is responsible directly to the Center Director.

Center Liaison

- The Center Liaison is accountable to the Center Director for the oversight of the CDER Research in Human Subjects program.
- The Center Liaison will conduct a final review of all CDER applications to conduct human subject research before submission to RIHSC.
- The Center Liaison will determine whether to recommend to the RIHSC that the research be exempt from RIHSC review.
- If the research is not eligible for exemption, the Center Liaison will determine the level of review needed by the RIHSC (Expedited or Full) and submit that recommendation to the RIHSC.
- The Center Liaison will develop and implement, with the Director of the Quality Management Staff, a CDER Quality Assurance (QA) Program for all CDER human subject research. This plan must include provisions for risk-based review and QA inspections of selected CDER RIHSC protocols.
- The Center Liaison will promptly report any protocol deviations, adverse events, or other significant information received through sponsors. This applies to intramural studies as well as those being conducted at other institutions.
- The Center Liaison will be copied on all correspondence to and from the RIHSC, and will be responsible for verifying and documenting compliance with any RIHSC actions (e.g., suspensions, terminations). If evidence of noncompliance with RIHSC directives cannot be resolved with the sponsor, this information will be forwarded to RIHSC and to the sponsor's supervisory chain until resolved.

CDER RIHSC Project Manager

- The project manager is the primary contact for questions regarding the RIHSC submission process.
- The project manager will conduct a preliminary review of all RIHSC applications for completeness and accuracy before review by the RIHSC Liaison and will resolve any deficiencies in the submission with the principal investigator or sponsor.
- The project manager will maintain paper and electronic records of all human subject research reviewed by the Center Liaison and RIHSC, including protocols, letters of approval and exemption, training records, and all relevant documents sent to or received from the RIHSC for a minimum of 3 years after completion of the research.

- The project manager will track all approval dates and CR dates and notify principal investigators and sponsors 3 months in advance of their CR renewal, to ensure that materials are submitted for review well in advance of the protocol expiration date.
- The project manager will maintain documentation that CDER employees involved in human subject research have received training in human subject protection rules and regulations.
- The project manager will assemble the final RIHSC application package, including preparation of all forms needed for the Center Liaison's review and signature.
- Upon request, the project manager will provide information to any CDER employee on how to receive required training in the regulations related to human subject research.

CDER Quality Assurance Staff, Office of Executive Operations

- CDER Quality Assurance Staff, Office of Executive Operations, monitors the Quality Systems Program to oversee the quality and risk assessment of all CDER-sponsored intra- and extramural activities on research involving human subjects. The objective of this program is to assure the quality and integrity of data and information from human subject research studies sponsored by CDER, and to ensure that there is adequate documentation that the research is being conducted in compliance with applicable regulations and policies.

Division Director of the Sponsor

- The sponsor's Division Director will ensure that the proposed research has been reviewed for scientific merit and mission relevance.
- The Division Director is responsible for, and must assure, oversight of the sponsor's activities. *Note: For sponsors who are at the Division Director level or higher, assurance from the Office Director is not required.*

CDER Employees (FDA Sponsor and/or Principal Investigator)

Before RIHSC submission

- All CDER employees involved in human subject research must read and be familiar with FDA Internal Operating Procedures for research involving human subjects which can be found in the reference section of this MAPP.
- All CDER employees conducting human subject research must complete training in the HHS regulations on human subject protection and must obtain a certification of completion before submitting a protocol for RIHSC review. If training has been completed at another institution, a certificate of completion should accompany the application. CDER employees who have not received training may contact OTS for training materials to complete this requirement, or take the on-line Investigator 101 course and quiz (see reference section).
- All CDER employees planning studies for which a Full or Expedited RIHSC Review is needed should contact the CDER RIHSC Liaison during the early planning stages. The sponsor must ensure that each expedited or full submission undergoes appropriate review for programmatic relevance, scientific merit, and/or statistical adequacy before submission to RIHSC.
- Should the human subject research require an IND, the CDER sponsor is responsible for filing the IND before submitting the protocol to RIHSC for review.

- All CDER employees who currently are, or plan to be, involved in human subject research must submit to the Center Liaison all materials and forms (listed under Procedures) detailing the research, as outlined below. All materials should be sent through the project manager in OTS.
- All CDER employees planning focus group testing or survey research requiring clearance through the Office of Management and Budget (OMB) must submit documents to the Center Liaison before submission to OMB. Obtaining OMB clearance is the responsibility of the sponsor.

Conduct of Study

- All CDER employees conducting human subject research must maintain all project data, study records, and all related documentation and correspondence. Study files are subject to QA audit by the RIHSC Liaison or the FDA Quality Assurance Board.
- All CDER sponsors for off-site studies are responsible for monitoring study conduct by maintaining close communication with the on-site PI to ensure that:
  - No changes to the protocol, study personnel, or informed consent are implemented until they are approved by **both** their local IRB and the RIHSC.
  - All adverse events or unexpected problems are promptly reported to the local IRB and the FDA Sponsor, as described in the RIHSC SOPs (see Reference section).
  - All actions initiated by the local IRB are promptly reported to the FDA Sponsor.
  - Copies of all official letters, approvals, and documents from the local IRB are forwarded to the FDA Sponsor (e.g., stamped, dated copies of all versions of the protocols and informed consent forms; all official approval letters).
  - All actions taken by the RIHSC are promptly communicated to the local PI and adhered to.
- All CDER sponsors are responsible for promptly forwarding all communications from the local IRB or PI to the RIHSC Liaison, including any adverse event reports, anticipated protocol changes, protocol deviations, or reports from the off-site PI.
- CDER employees are responsible for submitting CRs annually for protocols approved using expedited or full review procedures. Work on the protocol may not extend more than 1 year beyond previous review without written approval from the RIHSC.

Completion of the Study

- All CDER employees should notify the RIHSC Project Manager when a project has been completed, whether it was exempted or approved using Expedited or Full Review procedures. For all non-exempt protocols, a final report must be submitted to the RIHSC through the RIHSC Liaison.
- Change of Intent. If an employee has completed a purely regulatory project and now would like to incorporate the results into a research publication, a copy of the manuscript should be sent through the Center Liaison to the RIHSC for review before submission.
- All CDER employees who seek to publish the results of human subject research must document compliance with research involving human subject regulations. A copy of the exemption or approval letter signed by the FDA's RIHSC Chair must accompany the proposed manuscript when presented for clearance by the employee's Office Director.
- All CDER employees conducting human subject research must complete and maintain a record in the CDER Research Database at: http://10.118.6.12:591/CDER_Science. Principal Investigators should also ensure that publications resulting from the project are entered into the CDER Publications & Presentations Database at http://10.118.6.12:591/FDA_pubs_and_pres/CDER/.

PROCEDURES

- CDER employees should contact the project manager to obtain assistance in preparing a RIHSC submission package.

- All RIHSC submission documentation should be forwarded to the RIHSC Project Manager. The following forms and/or documentation are required by the RIHSC as part of the application package:

  All RIHSC forms listed below are available on-line on the RIHSC web page at http://inside.fda.gov/ProgramsInitiatives/Drugs/ScienceResearch/UCM035467.html.

  A. Concept Review

  Documents to be provided by the FDA Sponsor:
  - CDER Assurance Form
  - Copy of work proposed (e.g., RFP, Contract, IAG, MOU)
  - Curriculum vitae (CV) of Principal Investigator
  - Certification of completed Investigator 101 Course/Quiz (copy of confirmatory e-mail)
  - Division Director Assurance Form

  Documents to be prepared by the RIHSC Project Manager and signed by the RIHSC Liaison:
  - Certification of Exempt Status (RIHSC Form)
  - Transmittal Memo (RIHSC Form)

  B. Exempt Review Application

  Documents to be provided by the FDA Sponsor:
  - CDER Assurance Form *(to be signed by Division Director)*
  - Protocol or project description, including:
    - Short project summary
    - Description of how the data (or samples) have been de-identified
    - If tissue samples are involved, a description of their secure storage and disposition after the study is complete (e.g., will they be destroyed?)
    - If samples are coming from a clinical study at another site, a copy of the IRB approval letter (not the entire protocol)
    - If the exemption request is for a contract or other formal agreement, a copy of the agreement
  - Informed Consent form (if needed)
  - CV of Investigators and FDA Sponsor
  - Certification of completed Investigator 101 Course/Quiz (copy of confirmatory e-mail)

  Documents to be prepared by the RIHSC Project Manager and signed by the RIHSC Liaison:
  - Certification of Exempt Status (RIHSC Form)
  - Transmittal Memo (RIHSC Form)

  C. **Expedited and Full Review Application**

  Documents to be provided by the FDA Sponsor:
  - CDER Assurance Form (to be signed by Division Director)

- Protocol/Concept Submission Facesheet (RIHSC Form)
- CV of Investigators and FDA Sponsor
- Copy of Protocol or description of project
- Copy of Informed Consent (if applicable)
- Copy of any contracts or agreements for which RIHSC approval is being sought (if applicable)
- Certification of completed Investigator 101 Course/Quiz (copy of confirmatory e-mail)

Documents to be prepared by the RIHSC Project Manager:

- Application for an Expedited Review (if applicable) (RIHSC Form)
- Transmittal Memo (RIHSC Form)

D. **Continuing Review Application**

Documents to be provided by the FDA Sponsor:

- Continuing Review Application, with supporting documentation as needed (RIHSC Form)
- Current Protocol
- Current version of Informed Consent Form

Documents to be prepared by the RIHSC Project Manager:

- Application for an Expedited Review (if applicable) (RIHSC Form)
- Transmittal Memo (RIHSC Form)

- The CDER RIHSC Project Manager should be notified by the PI and/or FDA Sponsor when projects are completed, including those that are exempt.
- Following the completion of any nonexempt study, CDER employees must submit a Final Report to the RIHSC through the Liaison. The summary should include the following information:
  - Brief summary of the project status
  - Number of subjects approved by the RIHSC for inclusion in the study and the number actually enrolled into the study
  - Number of subjects who dropped out of the study
  - Summary of adverse events associated with the study
  - List of abstracts or publications, and/or a brief description of any available study results *(No RIHSC forms are required when submitting the Final Report.)*
- In addition, following completion of the project, CDER employees should include documentation of RIHSC compliance (e.g., copy of the exemption or approval letter signed by the FDA's RIHSC Chair) with any manuscripts being submitted for review that have resulted from approved RIHSC protocols.
  - The RIHSC Liaison or Project Manager will contact the employee should any additional information or documentation be needed to ensure CDER's compliance with human subject research policies.

AUTHORITY

- 45 CFR part 46
- 21 CRF part 46
- 21 CFR part 50
- 21 CFR part 312 (if investigational drug is used)
- 21 CFR part 812 (if investigational device is used)
- U.S. Department of Health and Human Services Federal-wide Assurance (FWA) for the Protection of Human Subjects for Domestic (U.S.) Institutions

EFFECTIVE DATE

This MAPP is effective upon date of publication