18.0 CONDUCTING EXPEDITED INITIAL REVIEW

18.1 OBJECTIVE

To describe the policies and procedures for conducting expedited initial review.

18.2 GENERAL DESCRIPTION

The Institutional Review Board (IRB) uses an expedited review process to review studies that meet the categories adopted by the Department of Health and Human Services (DHHS) or the Food and Drug Administration (FDA) that involve no greater than "minimal risk." The expedited applicability criteria, including the definition of "minimal risk" and federally mandated categories are attached. Expedited review procedures allow the IRB to review and approve studies that meet the criteria in the attached document without convening a meeting of the full IRB. The IRB Chair or his/her designee, one or more experienced reviewers from among the Medical IRB membership (regular and alternate members) or the Nonmedical IRB Expedited Review Subcommittee conducts expedited initial review.

The expedited reviewers only approve research that meets the federal criteria for approval as specified in 45 CFR 46.111 and 21 CFR 56.111. Also, expedited reviewers ensure that the study's informed consent process and documentation meets the requirements as specified in 45 CFR 46.116 and 21 CFR 50.25unless the IRB waives the requirements in accord with federal regulations (See Informed Consent SOPP).

Expedited reviewers exercise all of the authority of the IRB except that the reviewers may not disapprove the research. The IRB only disapproves a research activity in accord with non-expedited procedures set forth in the DHHS and FDA regulations.

The IRB agenda for convened meetings advises the IRB of research studies approved using expedited review procedures. Any member can request to review the entire IRB file for an expedited study.

18.3 RESPONSIBILITY

Execution of SOPP: IRB Chair, IRB Members, Office of Regulatory Research Compliance (ORRC) Staff, ORRC Research Compliance Officer (RCO), Principal Investigator (PI)/Study Personnel.

18.4 PROCEDURES

18.4.1 Assigning Reviewers

- Each year, after finalizing the list of IRB members, ORRC RCO selects and recommend experienced members from each IRB committee to serve as expedited reviewers. Members who have served on an IRB for three months qualify as an experienced member.

- ORRC staff makes initial Medical IRB reviewer and Nonmedical IRB Expedited Review Subcommittee assignments based on the member's familiarity with IRB issues, experience, and expertise and forward the proposed assignments to the respective IRB Chair for review and approval. ORRC staff forward the approved list of expedited reviewers to the IRB members.

- The expedited reviewer notifies ORRC staff if he/she is not available to conduct expedited review during the assigned time period or has a conflict of interest as outlined in the IRB Member and Consultant Conflict of Interest SOPP. ORRC staff document who served as expedited reviewer on the applicable reviewer form (i.e., Expedited Reviewer Worksheet).

18.4.2 Submission and Screening

- The PI makes a preliminary determination that a protocol is eligible for expedited review based on the criteria in the attached document. The IRB makes the final determination regarding whether a protocol is eligible for expedited review.

- The PI submits a completed expedited review application to the ORRC. Instructions for preparing the application are available on the ORRC website. The investigator may call the ORRC with questions.

- Upon receipt of the application, ORRC staff screen it for completeness and accuracy and make a preliminary determination that the application meets the criteria for expedited review, including minimal risk, and identifies the research categories. If the application does not meet the criteria for expedited review, ORRC staff advises the PI to resubmit the study for full or exempt review.

- ORRC staff follows the screening procedures outlined in the Initial Full Review SOPP (e.g., screening for vulnerable subjects or federally mandated specific findings; for waiver of informed consent or documentation requests; for completion of mandatory training requirements; for need of additional expertise or prisoner representative review). See the Initial Full Review SOPP for a detailed description of ORRC staff procedures.

- ORRC staff notes during the screening process that the proposal involves areas of research requiring federally mandated specific findings. ORRC staff

use the checklist of specific findings in the Expedited Reviewer Worksheet to alert the expedited reviewer(s) of the areas requiring determinations.

- ORRC staff also screens for Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule and/or Family Educational Rights and Privacy Act (FERPA) concerns. If the PI includes a HIPAA form or checks “HIPAA” in the application or if there are any HIPAA or FERPA concerns, ORRC staff forwards the application to the HIPAA Compliance Officer for review. The HIPAA compliance officer reviews the application and submits suggestions in writing/email. ORRC staff forward these suggestions to the IRB Chair, the medical expedited reviewer, or the Nonmedical IRB Expedited Review Subcommittee for a final determination.

- ORRC staff enters the application into the ORRC protocol database tracking system and assigns a number to the application.

- After completing application screening, ORRC staff retains the original application in the ORRC and send a copy of the application to the expedited reviewer(s).

- The IRB Chair, one or more experienced reviewers from the Medical IRB (regular and alternate members), or the Nonmedical IRB Expedited Review Subcommittee conducts expedited initial review.

18.4.3 Nonmedical IRB Expedited Review Process

- A Nonmedical IRB Expedited Review Subcommittee, comprised of the Chair, Vice Chair, and two IRB members will conduct expedited reviews.

- ORRC staff sends the materials to the subcommittee members for review. The ORRC provides an electronic copy of the detailed protocol/grant application for review by one of the subcommittee members following primary review procedures.

- However, this member may not vote unless he/she has had the opportunity to review the same materials as those sent to the subcommittee. The subcommittee may review and approve protocols as long as one voting IRB member is present (i.e., Chair, Vice Chair, or any of the designated IRB subcommittee members).

- The subcommittee, with assistance from ORRC staff, documents federally mandated specific findings (e.g., Subpart B, C, D, or waiver of informed consent or documentation) and controverted issues by completing the Expedited Reviewer Worksheet and/or by inclusion of discussion in the minutes of the convened meeting. In conducting the initial review of the

proposed research, the subcommittee utilizes the Criteria for IRB Approval: Reviewer Checklist.

- If an investigator needs an expedited review prior to a convened meeting, the Nonmedical IRB Chair, Vice Chair, or any experienced member (i.e., regular or alternate) may serve as the expedited reviewer following the same procedures as those used for the Medical IRB expedited review process.

18.4.4 Medical IRB Expedited Review Process

- For the Medical IRB, the primary expedited reviewer conducts expedited reviews outside of a convened meeting. If the primary expedited reviewer is not available or has a conflict of interest, the ORRC contacts a secondary reviewer to conduct the review.

- The designated ORRC staff sends the primary expedited reviewer recommendations for the appropriate expedited category and justification for the chosen category(s).

- The ORRC sends the application materials to the primary expedited reviewer on the Medical IRB. If the reviewer is unable to respond within approximately 7 days, ORRC staff sends the reviewer up to two reminders. If the expedited reviewer still does not respond, ORRC staff forward the protocol to the secondary reviewer.

- The expedited reviewer contacts the PI for any clarification needed and documents the issues discussed on the Expedited Reviewer Worksheet. The expedited reviewer also utilizes the Criteria for IRB Approval: Reviewer Checklist to document that the research meets the federal criteria for IRB approval. The expedited reviewer makes determinations for specific findings using the information from the IRB application and records his/her determinations on the Expedited Reviewer Signature Page.

- The reviewer also documents any issues pertaining to special findings (e.g., requests for waiver of informed consent or documentation) through the materials submitted by the PI and the expedited reviewer's final approval of the application. The reviewer only raises controverted issues that he/she has determined do not meet the federal criteria for approval or HU IRB policies.

18.4.5 Materials Sent to Medical and Nonmedical IRB Reviewers

- Both the medical and nonmedical expedited reviewers receive the following IRB application materials and IRB forms:
  - Application, Expedited Review Worksheet with review categories, and Research Description;

- Informed consent/assent process and forms, including waiver requests, NIH sponsored cooperative group trial forms, translated consent document for non-English speaking subjects;
- HIPAA forms;
- Additional materials, including advertisements, proposal data instruments, materials/letters for off-site research, Use of Investigational New Drug (IND) Form, Use of Approved Drugs for Unapproved Use Form, Use of Radioactive Materials Form;
- Vulnerable populations, including forms for research involving individuals with *impaired decision-capacity,* fetuses and/or neonates, prisoners, or children, *and economically or educationally disadvantaged persons*;
- Criteria for IRB Approval: Reviewer Checklist;
- ORRC staff comments/recommendations, if applicable.

- Expedited reviewers review all information in the expedited review folder in enough depth to be familiar with the protocol, to determine whether the research is eligible for expedited review, and to determine whether the research meets the regulatory criteria for approval.

18.4.6 Review Outcomes

- Both medical and nonmedical expedited reviewers make the final determination as to whether research activities meet the expedited review criteria outlined in the attached document.

- The reviewer can also recommend that the activities do not fall under IRB purview. In these cases, the IRB handles the review using procedures outlined in the Determination of Activities That Need IRB Review SOPP.

- The reviewers also determine whether the research meets the federal criteria for approval as outlined in 45 CFR 46.111 and 21 CFR 56.111.

- Expedited reviewers also ensure that the investigator will conduct the informed consent process and obtain documentation of informed consent, as specified in 45 CFR 46.116 and 117 and 21 CFR 50.25, unless the IRB

waives the requirements in accord with federal regulations (See Informed Consent SOPP).

- The expedited reviewers only raise those controverted issues or request changes that they have determined do not meet the federal criteria for approval or HU IRB policies.

- The expedited reviewers document on the Expedited Reviewer Worksheet their determinations regarding expedited eligibility, applicable expedited category, and whether the research meets the federal criteria for approval.

- The expedited reviewers make one of the following three determinations in regard to the protocol and consent forms:
  - APPROVED: IRB approval indicates that the IRB reviewer(s) has concluded that the research and consent forms meet the federal criteria for approval. An IRB approval vote verifies that the IRB agrees with the assessment of the protocol and/or specific findings as described by the PI in the application. ORRC staff sends the investigator an approval notification according to the guidelines in the ORRC Customer Service Standard, accompanied by an informed consent/assent document with the affixed "IRB Approval" validation stamp which includes valid dates of IRB approval. Upon request, ORRC staff also sends the PI a funding agency Certification of Approval form.
  - APPROVED/ACCEPTED with ADMINISTRATIVE REVIEW: That the IRB member reviewing the protocol has approved the protocol pending submission of minor revisions/information: In this case, the member has given the compliance staff the authority to approve the minor revisions which do not involve substantive concerns. The PI responds to the board member's suggested revisions in writing and sends the response to the ORRC, validation and approval.
  - REVISIONS and/or ADDITIONAL INFORMATION REQUIRED: The IRB reviewer(s) withhold approval pending submission of revisions/additional information. ORRC staff sends the investigator a notification letter according to the guidelines in the ORRC Customer Service Standards, describing the revisions requested by the IRB expedited reviewers. The PI responds to revisions requested by the IRB in writing and sends the response to the ORRC. ORRC staff forward those responses to the expedited reviewer for further review.
  - FULL REVIEW REQUIRED: The IRB expedited reviewers may determine that the protocol requires full review by the IRB at a convened meeting.

- The medical and nonmedical expedited reviewer(s) can determine that the research is eligible for a less stringent mechanism of review (i.e., the project is exempt from requirements for review or the activities do not fall under the purview of the IRB). In these cases, the IRB does not require a new application provided the IRB, with assistance from ORRC staff, documents

the exempt categories or the rationale for determining that the activities do not meet the federal definitions of research, clinical investigation, or human subject.

- The ORRC procedures for notifying the PI of the review outcome, obtaining follow up correspondence, and issuing approval notification letters outlined in the Initial Full Review SOPP apply for expedited review as well. See Initial Full Review SOPP for details.

- Once the IRB reviewer(s) approves the study, the ORRC staff and the RCO designee assigns the approval period at intervals appropriate to the degree of risk but not less than once per year. The date the expedited reviewer signs off final approval on the study is the date the approval period starts. ORRC staff document the approval period dates in the approval letter to the PI.

- If the PI has concerns regarding the IRB decision/recommendations for changes in the study, he/she may submit his/her concerns to the IRB reviewer via a written document that includes justification for changing the IRB decision. The PI sends the request to the expedited reviewer and/or to the IRB Chair or Vice Chair for final resolution. If the investigator is still dissatisfied with the IRB decision, ORRC staff sends the protocol to the convened IRB for review.

18.4.7 Federally Mandated Expedited Review Criteria – Effective November 9, 1998 – Definition of Minimal Risk Guidance to PI and Reviewers

- Expedited procedures can only be used to review a study if the only involvement of human subjects fits one or more of the categories specified in the federal regulations and if all of the procedures present no greater than "minimal risk."

- The IRB reviewer confirms that **all of the research activities** fit in one or more of the expedited categories. If the research includes activities that do not fit in the categories, the study is not eligible for expedited review even if the research involves "minimal risk."

- The Department of Health and Human Services defines *minimal risk* to mean "the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests" [45 CFR 46.102(2)(i)].

- Investigators are asked to provide a risk assessment, but it is the IRB reviewer's responsibility to determine whether the research meets the federal definition.

- The IRB reviewer must consider two questions:
  - Is the probability of the harm or discomfort anticipated in the proposed research greater than that encountered ordinarily in daily life or during the performance of routine physical or psychological examinations or tests? OR
  - Is the magnitude of the harm or discomfort greater than that encountered ordinarily in the daily life or during the performance of routine physical or psychological examinations or tests?

- If the answer is "yes" to either of these questions, then the research does not meet the definition of minimal risk. The IRB policy on risk assessment is included in the HU Assessing the Research Risk document, which is on the ORRC website and in the IRB Survival Toolkit.

18.4.8 Federal Expedited Review Applicability and Categories

- Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

- The categories in this list apply regardless of the age of subjects, except as noted.

- The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

- The expedited review procedure may not be used for classified research involving human subjects.

- IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review—expedited or convened—utilized by the IRB.

- Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

18.4.9 Research Categories

- Clinical studies of drugs and medical devices only when condition (a) or (b) is met:
  - Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review).
  - Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

- Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
  - From healthy non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
  - From other adults and children1 considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

- Prospective collection of biological specimens for research purposes by noninvasive means. Examples: (a) Hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum-based or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

- Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing (Studies intended to evaluate the safety and effectiveness of the medical device are not

generally eligible for expedited review, including studies of cleared medical devices for new indications). Examples: (a) Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

- Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis) (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt).

- Collection of data from voice, video, digital, or image recordings made for research purposes.

- Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects 45 CFR 46.101 (b)(2) and (b)(3) -- This listing refers only to research that is not exempt).

- Continuing review of research previously approved by the convened IRB as follows:
  - Where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
  - Where no subjects have been enrolled and no additional risks have been identified; or
  - Where the remaining research activities are limited to data analysis.

- Continuing review of research not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

18.5 REFERENCES

21 CFR 56.102(i)
21 CFR 56.110
45 CFR 46.102(i)
45 CFR 46.110
63 FR 60364-60367; 63 FR60353 – 60356 DHHS-FDA lists published in Federal Register November 9, 1998