

GCP Requirements: IRB /IEC

DMID/ICSSC

11/20/09

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IRB/IEC

Responsibilities

- ◆ To protect rights, safety and well-being of participants

IRB/IEC

Membership

- ◆ At least 5 members
- ◆ Diversity of the members
 - Race
 - Gender
 - Cultural background
 - At least one scientist
 - At least one non-scientist
 - At least one members who is not from the institution
 - No conflict of interest

IRB/IEC

Membership

- ✦ Sensitive to needs and concerns of the community
- ✦ Sensitive to special issues concerning vulnerable populations (e.g., prisoners, children, pregnant women)
- ✦ May invite people with special competence to provide advice

IRB/IEC

IRB Review of Research:

- ◆ Conduct initial and continuing review of research
- ◆ Review research at convened meetings at which majority of members are present, including at least one non-scientist

IRB/IEC

Expedited Review:

- ◆ Includes projects where the risk to subject are no more than minimal OR
- ◆ Minor changes in previously approved research
- ◆ Carried out by IRB Chair or one or more experienced reviewers

IRB/IEC

Criteria for IRB/IEC review:

- ◆ Risks to subjects are minimized
- ◆ Risks are reasonable in relation to anticipated benefits
- ◆ Selection of subjects is equitable
- ◆ Informed consent obtained and documented
- ◆ Monitoring of data
- ◆ Confidentiality of data and privacy of subjects

IRB/IEC

Review outcomes:

- approve
- require modifications
- disapprove

IRB/IEC

What does initial review of research entail?

- Protocol
- Informed Consent Forms
- Recruitment procedures (e.g., advertisements)
- Written information given to subjects
- Investigator's Brochure
- Safety information
- CV of Investigator
- Information about payments to subjects
- Other documents can be requested

IRB/IEC

Continuing review of research:

- ◆ At intervals appropriate to the degree of risk
- ◆ Not less than once a year
- ◆ Should be done at convened meetings except if eligible for expedited review
 - When is this permissible?

IRB/IEC

What does continuing review entail?

- ◆ **All IRB Members should receive:**
 - Protocol Summary
 - Progress report on status of research, including:
 - Number of subjects accrued
 - Summary of AEs and any unanticipated problems involving risks to subjects and any withdrawal of subjects from research
 - Summary of relevant information, especially safety information
 - Informed consent form(s)

- ◆ **At least one IRB member should receive complete protocol including previously approved modifications**

IRB/IEC

How is continuing review date determined?

- ◆ Continuing review must occur “on or before the date when IRB approval expires”
- ◆ Focus on date of convened meeting at which IRB approval was granted and NOT date of letter
- ◆ Review of a change in a protocol does not alter the continuing review due date

IRB/IEC

Examples:

1. An IRB reviews and approves a protocol at a convened meeting on 15 September, 2006. Continuing review must occur by 15 September, 2007.
2. IRB approves a protocol at a convened meeting on 15 September 2007.
 - Protocol amendment is approved on 30 November 2007.
 - Continuing review must occur by 15 September, 2008.

IRB/IEC

What occurs if there is a lapse in continuing review?

- ✦ The research must STOP, unless the IRB finds that it is in the best interests of subjects to continue participate in the research
- ✦ Enrollment of new subjects cannot occur

IRB/IEC

IRB/IEC records

- Copies of protocols and informed consent forms
 - Minutes of meetings
 - Records of continuing review
 - Correspondence with investigators
 - List of IRB/IEC members
- ◆ **IRB/IEC records to be retained for 3 years after completion of study**

IRB/IEC

RE: [REDACTED], Version 3.0: A Phase III, [REDACTED]

The Committee on Human Research has reviewed and approved this application to involve humans as research subjects. This included a review of all documents attached to the original copy of this letter.

Specifically, the review included but was not limited to the following documents:

Tissue Bank Consent Form, Dated 9/15/04

Screening Consent Form, Dated 9/16/04

Enrollment Consent Form, Dated 4/24/06

Ancillary Tissue Bank Consent Form, Dated 11/15/04

Ancillary Consent Form, Dated 11/11/04

The [REDACTED] is the Institutional Review Board (IRB) for [REDACTED] and its affiliates. [REDACTED] holds Office of Human Research Protections Federalwide Assurance number [REDACTED]. See the [REDACTED] website for a list of other applicable FWAs.

APPROVAL NUMBER: H9425-23329-04. This number is a [REDACTED] [REDACTED] number and should be used on all correspondence, consent forms and patient charts as appropriate.

APPROVAL DATE: August 17, 2006

EXPIRATION DATE: August 17, 2007

Full Committee Review

IRB/IEC

[REDACTED]
[REDACTED]

25 October 2006

Our Ref: 009-04-02

[REDACTED]

Dear [REDACTED],

RE: SUBMISSION FOR ANNUAL CONTINUING REVIEW FOR THE PROTOCOL:

[REDACTED]
[REDACTED] (Protocol version 2.0, dated 02 August 2004)

We acknowledge receipt of your letters dated 10 October 2006 (for information purposes only), 16 October 2006 and Progress Report Form dated 16 October 2006.

In the consent form, please note that an illiterate participant should be witnessed by someone who is literate.

Ethical clearance is approved for a further year. This approval expires 7 December, 2007.

Yours sincerely

Implementation of GCP Requirements: IRB/IEC Exercise

1. If study sites distribute gift bags (containing t-shirts, pens, mugs, and caps) to subjects, would IRB/IEC review be necessary?
2. If a video presentation is used to supplement the informed consent process, must the IRB/IEC first review and approve the presentation?
3. Must a questionnaire that assesses a subject's comprehension of the consent be submitted to the IRB/IEC for review?
4. A protocol was initially approved on 1 April 2004. The investigator submitted the amendment and revised consent forms to the IEC and received approval on 30 May 2004.

The investigator requested continuing review approval from the IEC on 28 April 2005 and was granted renewed approval by the ethics committee on 15 June 2005.

What errors were made, if any, in this case study and who made them?

Telephone: [REDACTED]
Telefax: [REDACTED]
E-mail: [REDACTED]
Website: [REDACTED]



[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

[REDACTED]

Ref: [REDACTED]

Date: 3 May 2007

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

RE: Phase II/II b Safety and effectiveness study of the Vaginal Microbicide Buffer Gel and 0.5% PRO 2000/5 Gel (P) for prevention of HIV infection in Women MRCZ/A/1135

Thank you for the Application for Continuing Review of Research Activity and Progress Report that you submitted for review to the [REDACTED] Research Council of Zimbabwe (MRCZ). Please be advised that the [REDACTED] Research Council of Zimbabwe has reviewed and approved your application to continue conducting the above titled study. This approval is based on;

- HPTN 035 Protocol version 2.0 Dated 02 August 2004
- HPTN 035 Progress Report
- Informed Consent Forms dated 15 February 2006

• **APPROVAL NUMBER** [REDACTED] A/1135

This number should be used on all correspondence, consent forms and documents as appropriate.

- **APPROVAL DATE** : 3 May 2007
- **MEETING DATE** : 3 May 2007
- **TYPE OF MEETING** : FULL BOARD
- **EXPIRATION DATE** : This approval expires on 2 May 2008.

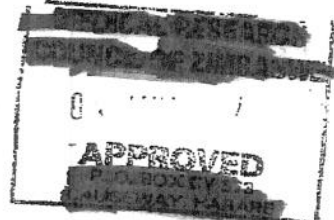
After this date, this project may only continue upon renewal. For purposes of renewal, a progress report on a standard form obtainable from the [REDACTED] Offices should be submitted one month before the expiration date for continuing review

- **SERIOUS ADVERSE EVENT REPORTING:** All serious problems having to do with subject safety must be reported to the [REDACTED] Research Council of Zimbabwe (MRCZ) as well as the [REDACTED] within 3 working days using standard forms obtainable from the [REDACTED] Offices.
- **MODIFICATIONS:** Prior [REDACTED] and [REDACTED] approval using standard forms obtainable from the [REDACTED] Offices is required before implementing any changes in the Protocol (including changes in the consent documents)
- **TERMINATION OF STUDY:** On termination of a study, a report has to be submitted to the [REDACTED] using standard forms obtainable from the [REDACTED] Offices.
- **QUESTIONS:** Please contact the [REDACTED] on Telephone No. [REDACTED] or by e-mail on [REDACTED]

- **Other:**
Please be reminded to send in copies of your final research results for our records as well as for the [REDACTED] Research Database.

Kind regards from the [REDACTED]

[REDACTED]



PROMOTING THE ETHICAL CONDUCT OF HEALTH RESEARCH
Registered with the USA Office for Human Research Protections (OHRP) as an International IRB

[REDACTED]

Tel: [REDACTED]
[REDACTED] (General)
Fax: [REDACTED]
Email: [REDACTED]
[REDACTED]



[REDACTED]
INSTITUTE
[REDACTED]

Our Ref: [REDACTED]
Your Ref:

September 11, 2007

Dr. [REDACTED]

RE: CHAY 002: PROSPECTIVE STUDY OF THE DETERMINANTS OF HOST RESISTANCE TO HIV INFECTION, Version 1.0, June 8, 2006

Thank you for submitting the above progress report dated September 04, 2007 to the [REDACTED] Science and Ethics Committee.

I am happy to inform you that after review of the submitted report, approval has been given today September 11, 2007 for you to continue with the study for another twelve months starting on October 21, 2007 up to October 20, 2008:

You are reminded that this approval is for one year and you are expected to request for renewal, if applicable, one month before October 20, 2008.

I wish you all the best with the study.

Sincerely,

[REDACTED]
[REDACTED]

Cc: Chairman SHC
Cc: Director UVR
Cc: Secretary SEC

**Office for Human Research Protections
Department of Health and Human Services**

Guidance on Continuing Review

This guidance represents OHRP's current thinking on this topic and should be viewed as recommendations unless specific regulatory requirements are cited. The use of the word *must* in OHRP guidance means that something is required under HHS regulations at 45 CFR part 46. The use of the word *should* in OHRP guidance means that something is recommended or suggested, but not required. An institution may use an alternative approach if the approach satisfies the requirements of the HHS regulations at 45 CFR part 46. OHRP is available to discuss alternative approaches at 240-453-6900 or 866-447-4777.

Date: January 15, 2007

Scope: This document describes the requirements of Department of Health and Human Services (HHS) regulations at 45 CFR 46.109(e) for the continuing review of human subjects research by an Institutional Review Board (IRB) at intervals appropriate to the degree of risk, but not less than once per year. In particular, OHRP offers guidance on the following topics:

1. what constitutes substantive and meaningful continuing review;
2. what are some additional considerations for continuing review of multi-center trials monitored by a Data and Safety Monitoring Board (DSMB), Data Monitoring Committee (DMC), other similar body, or sponsor;
3. when may expedited review procedures be used for continuing review;
4. how is the continuing review date determined;
5. what occurs if there is a lapse in continuing review; and
6. what is the required composition of IRBs specifically designated to conduct continuing review.

Target Audience: IRBs, investigators, research institutions, and sponsors.

REGULATORY REQUIREMENTS

The HHS regulations for the protection of human subjects ([45 CFR Part 46](#)) require that, among other things, (1) institutions have written procedures which the IRB will follow for (a) conducting its continuing review of research and for reporting its findings and actions to investigators and the institution, and (b) determining which projects require review more often than annually (45 CFR 46.103(b)(4)); (2) except when an expedited review procedure is used, each IRB reviews proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in the nonscientific areas (45 CFR 46.108(b)); and (3) an IRB conducts continuing review of research at intervals appropriate to the degree of risk, but not less often than once a year (45 CFR 46.109(e)).

WHAT CONSTITUTES SUBSTANTIVE AND MEANINGFUL CONTINUING REVIEW?

Continuing review of research must be substantive and meaningful. In accordance with HHS regulations at 45 CFR 46.108(b) and at 46.115(a)(2), continuing review by the convened IRB, with recorded vote on each study, is required unless the research is otherwise appropriate for expedited review under Section 46.110 (see below). Furthermore, HHS regulations at 45 CFR 46.111 set forth the criteria that must be satisfied in order for the IRB to approve research. These criteria include, among other things, determinations by the IRB regarding risks, potential benefits, informed consent, and safeguards for human subjects. The IRB must ensure that these criteria are satisfied at the time of both initial and continuing review. In particular, when conducting continuing review, the IRB needs to determine whether any new information has emerged either from the research itself or from other sources that could alter the IRB's previous determinations, particularly with respect to risk to subjects. Of note, information regarding any unanticipated problems involving risks to subjects or others (hereinafter referred to as unanticipated problems) that have occurred since the previous IRB review in most cases will be pertinent to the IRB's determinations at the time of continuing review.

The procedures for continuing review by the convened IRB may include a primary reviewer system.

In conducting continuing review of research not eligible for expedited review, all IRB members should at least receive and review a protocol summary and a status report on the progress of the research that includes:

- the number of subjects accrued;
- a summary of any unanticipated problems and available information regarding adverse events (in many cases, such a summary could be a simple brief statement that there have been no unanticipated problems and that adverse events have occurred at the expected frequency and level of severity as documented in the research protocol, the informed consent document, and any investigator brochure);
- a summary of any withdrawal of subjects from the research since the last IRB review;
- a summary of any complaints about the research since the last IRB review;
- a summary of any recent literature that may be relevant to the research and any amendments or modifications to the research since the last IRB review;
- any relevant multi-center trial reports;
- any other relevant information, especially information about risks associated with the research; and
- a copy of the current informed consent document and any newly proposed consent document.

At least one member of the IRB (i.e., a primary reviewer) also should receive a copy of the complete protocol including any modifications previously approved by the IRB. Furthermore, upon request, any IRB member also should have access to the complete IRB protocol file and relevant IRB minutes prior to or during the convened IRB meeting.

When reviewing the current informed consent document(s), the IRB should ensure the following:

- The currently approved or proposed consent document is still accurate and complete;
- Any significant new findings that may relate to the subject's willingness to continue participation are provided to the subject in accordance with HHS regulations at 45 CFR 46.116(b)(5).

Review of currently approved or newly proposed consent documents must occur during the scheduled continuing review of research by the IRB, but informed consent documents should be reviewed whenever new information becomes available that would require modification of information in the informed consent document.

Furthermore, the minutes of IRB meetings should document separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB.

When reviewing research under an expedited review procedure, the IRB Chair (or designated IRB member(s)) should receive and review all of the above-referenced documentation, including the complete protocol.

WHAT ARE SOME ADDITIONAL CONSIDERATIONS FOR CONTINUING REVIEW OF MULTI-CENTER TRIALS MONITORED BY A DSMB, DMC, OTHER SIMILAR BODY, OR SPONSOR?

As noted above, continuing review of research by the IRB should include consideration of, among other things, unanticipated problems, adverse events, and any recent literature that may be relevant to the research.

OHRP recognizes that local investigators participating in multicenter clinical trials usually are unable to prepare a meaningful summary of adverse events for their IRBs because study-wide information regarding adverse events is not readily available to them. In such circumstances, when the clinical trial is subject to oversight by a monitoring entity (e.g., the research sponsor, a coordinating or statistical center, or a DSMB/DMC), OHRP recommends that at the time of continuing review local investigators submit to their IRBs a current report from the monitoring entity. OHRP further recommends that such reports include the following:

- (1) a statement indicating what information (e.g., study-wide adverse events, interim findings, and any recent literature that may be relevant to the research) was reviewed by the monitoring entity;
- (2) the date of the review; and
- (3) the monitoring entity's assessment of the information reviewed.

It may also be appropriate for the IRB at the time of continuing review to confirm that any provisions under the previously approved protocol for monitoring study data to ensure safety of subjects have been implemented and are working as intended (e.g., the IRB could require that the investigator provide a report from the monitoring entity described in the IRB-approved protocol).

WHEN MAY EXPEDITED REVIEW PROCEDURES BE USED FOR CONTINUING REVIEW?

The HHS human subjects regulations at 45 CFR 46.110(b)(1) limit the use of expedited review procedures to specific research categories published in the Federal Register at 63 FR 60364-60367 (see <http://www.hhs.gov/ohrp/humansubjects/guidance/63fr60364.htm>), and to the review of minor changes in previously approved research during the period (of one year or less) for which approval is authorized. IRBs are permitted to use expedited review for the continuing review of research that involves solely one or more of the activities published at 63 FR 60364-60367.

Generally, if research did not qualify for expedited review at the time of initial review, it does not qualify for expedited review at the time of continuing review, except in limited circumstances described by expedited review categories (8) and (9) at 63 FR 60364-60367. It is also possible that research activities that previously qualified for expedited review in accordance with HHS regulations at 45 CFR 46.110, have changed or will change, such that expedited IRB review would no longer be permitted for continuing review.

Expedited Review Category (8):

Under Category (8), an expedited review procedure may be used for the continuing review of research previously approved by the convened IRB as follows:

- (a) 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
- (b) Where no subjects have been enrolled and no additional risks have been identified; **OR**
- (c) Where the remaining research activities are limited to data analysis.

Of note, category (8) identifies three situations in which research that is greater than minimal risk and has been initially reviewed by a convened IRB may undergo subsequent continuing review by the expedited review procedure.

For a multi-center protocol, an expedited review procedure may be used by the IRB at a particular site whenever the conditions of category (8)(a), (b), or (c) are satisfied for that site. However, with respect to category 8(b), while the criterion that "no subjects have been enrolled" is interpreted to mean that no subjects have ever been enrolled at a particular site, the criterion that "no additional risks have been identified" is interpreted to mean that neither the investigator nor the IRB at a particular site has identified any additional risks from any site or other relevant source.

Expedited Review Category (9):

Under Category (9), an expedited review procedure may be used for continuing review of research not conducted under an investigational new drug application or investigational device exemption where categories (2) through (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.

The determination that "no additional risks have been identified" does not need to be made by the convened IRB.

HOW IS THE CONTINUING REVIEW DATE DETERMINED?

HHS regulations at 45 CFR 46.108(b) and 109(e) require, respectively, that (1) except when an expedited review procedure is used, each IRB must review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas; and (2) an IRB must conduct continuing review of research at intervals appropriate to the degree of risk, but not less frequently than once per year. The IRB should decide the frequency of continuing review for each study protocol necessary to ensure the continued protection of the rights and welfare of research subjects.

Several scenarios for determining the date of continuing review apply for protocols reviewed by the IRB at a convened meeting. To determine the date by which continuing review must occur, focus on the date of the convened meeting at which IRB approval occurs. (These examples presume the IRB has determined that it will conduct continuing review no sooner than within 1 year).

Scenario 1: The IRB reviews and approves a protocol without any conditions at a convened meeting on October 1, 2002. Continuing review must occur within 1 year of the date of the meeting, that is, by October 1, 2003.

Scenario 2: The IRB reviews a protocol at a convened meeting on October 1, 2002, and approves the protocol contingent on specific minor conditions the IRB chair or his/her designee can verify. On October 31, 2002, the IRB chair or designee confirms that the required minor changes were made. Continuing review must occur within 1 year of the date of the convened IRB meeting at which the IRB reviewed and approved the protocol, that is, by October 1, 2003.

Scenario 3: The IRB reviews a study at a convened meeting on October 1, 2002, and has serious concerns or lacks significant information that requires IRB review of the study at subsequent convened meetings on October 15 and October 29, 2002. At their October 29, 2002 meeting, the IRB completes its review and approves the study. Continuing review must occur within 1 year of the date of the convened meeting at which the IRB reviewed and approved the protocol, that is, by October 29, 2003.

Expedited Review

For a study approved under expedited review, continuing review must occur within 1 year of the date the IRB Chair or IRB member(s) designated by the Chair gives final approval to the protocol.

Review of a change in a protocol ordinarily does not alter the date by which continuing review must occur. This is because continuing review is review of the full protocol, not simply a change to it.

The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of research must occur on or before the date when IRB approval expires. OHRP recognizes the logistical advantages of keeping the IRB approval period constant from year to year throughout the life of each project. When continuing review occurs annually and the IRB performs continuing review within 30 days before the IRB approval period expires, the IRB may retain the anniversary date as the date by which the continuing review must occur. This would be, for example, October 1, 2003, in the above Scenarios 1 and 2, and October 29, 2003, in Scenario 3, even if the continuing reviews took place up to 30 days prior to these dates.

WHAT OCCURS IF THERE IS A LAPSE IN CONTINUING REVIEW?

The IRB and investigators must plan ahead to meet required continuing review dates. If an investigator has failed to provide continuing review information to the IRB or the IRB has not reviewed and approved a research study by the continuing review date specified by the IRB, the research must stop, unless the IRB finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions. Enrollment of new subjects cannot occur after the expiration of IRB approval.

When continuing review of a research protocol does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically. Such expiration of IRB approval does not need to be reported to OHRP as a suspension of IRB approval under HHS regulations.

WHAT IS THE REQUIRED COMPOSITION OF IRBS SPECIFICALLY DESIGNATED TO CONDUCT CONTINUING REVIEW?

OHRP is aware that some institutions have designated one or more IRBs for the sole purpose of conducting continuing review. While OHRP acknowledges that such a practice is permissible under the HHS regulations for the protection of human subjects, OHRP reminds institutions that such IRBs must comply with the IRB membership requirements stipulated by HHS regulations at 45 CFR 46.107. In particular, HHS regulations at 45 CFR 46.107(a) require the following for all IRBs, including IRBs that are solely responsible for continuing review:

The IRB must have at least five members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB must be sufficiently qualified through the experience and expertise of its members, and the diversity of members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB must therefore include persons knowledgeable in these areas. If the IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.

In addition, it should be noted that the other requirements for IRB membership at 45 CFR 46.107(b)-(f) also apply to IRBs conducting continuing review.

OTHER PERTINENT REGULATIONS

For FDA-regulated research, see 21 CFR 50, and 21 CFR 56.

**Categories of Research That May Be Reviewed by the
Institutional Review Board (IRB) through an
Expedited Review
Procedure¹**

Applicability

(A) 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.

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

(C) 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.

(D) The expedited review procedure may not be used for classified research involving human subjects.

(E) 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.

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

Research Categories

(1) Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

(a) 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.)

(b) 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.

(2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

(a) from healthy, nonpregnant 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

(b) from other adults and children², 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.

(3) 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 gumbase 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.

(4) 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.

(5) 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.)

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

(7) 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.)

(8) Continuing review of research previously approved by the convened IRB as follows:

(a) 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

(b) where no subjects have been enrolled and no additional risks have been identified; or

(c) where the remaining research activities are limited to data analysis.

(9) 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.

¹ An expedited review procedure consists of a review of research involving human subjects by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB in accordance with the requirements set forth in [45 CFR 46.110](#).

² Children are defined in the HHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." [45 CFR 46.402\(a\)](#).

Source: 63 FR 60364-60367, November 9, 1998.

Exercise: IRB/IEC

Group A:

You are an investigator preparing to implement an avian influenza study in Egypt. Write a letter to your local ethics committee seeking initial approval of the study. Hint: refer to the DMID Regulatory File Guidelines for the identifiers that must be included in the submission letter.

Group B:

You are the chairperson of an ethics committee. An investigator submitted documentation to the ethics committee seeking initial approval of the study (the study is NOT a minimal risk study). Write a letter to the investigator informing him of the outcome (approve/require modifications/disapprove) of the review of the study. Hint: refer to the DMID Regulatory File Guidelines for the identifiers that must be included in the letter. In addition, refer to the slide presentation and recall the discussion of IRB/IEC approval letters.

SUBMISSION LETTER/SUBMISSION PACKAGE/IRB/IEC APPROVAL

This section (or alternate location if other file system is used) must include a copy of the original IRB/IEC approved Protocol for the study and any subsequent IRB/IEC approved revisions/amendments to the Protocol. Include full copies of all final versions – newest in front.

Starting with the original Protocol and each Protocol revision or amendment afterward, maintain the ENTIRE PACKET PHYSICALLY TOGETHER in the file – the submission letter, submission package, any response to stipulations, comments, or questions, and the final IRB/IEC Approval.

All documents must have a Version number and date. Suggestion for all IRB/IEC submissions: The memo to the IRB/IEC should state clearly what documents are being submitted for review, including Version number and date of all Protocol, Informed Consents, advertisements, and amendments. If known, also include the date of the IRB/IEC review meeting.

To facilitate verification of regulatory compliance, DMID recommends that the following bulleted items be identified in the IRB/IEC Approval letter. If these elements are not included in the Approval letter, please write a note to the file indicating the items approved, including Version and date of all submitted documents.

- At a minimum, the IRB/IEC Approval letter should contain the following, per GCP Guideline 3.1.2:
 - DMID Protocol name and number, clearly identifying the trial
 - Approval date
 - A list of the documents approved
- In addition, DMID suggest these be included:
 - IRB/IEC chairperson or designee's signature
 - Should be addressed to the PI
 - Should list all sites covered by IRB/IEC Approval
 - Version number and date of documents submitted

Note: If contingent Approval is granted, evidence of final Approval must be present before the study can be implemented.