#### New and Continuing IRB Review

#### §46.111 Criteria for IRB approval of research.

(a) In order to approve research the IRB shall determine that all of the following requirements are satisfied:

1. Risks to subjects are minimized: (i) By using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk, and (ii) Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
3. Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and the IRB should be particularly cognizant of the special problems of research that involves a category of subjects who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.
4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by §46.116.
5. Informed consent will be appropriately documented, or documentation is waived in accordance with §46.117.
6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(b) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, NYU employees/students or economically disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

## Guidance on Continuing Review

### 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 46.108(a)(3)); (2) , 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 covered at intervals appropriate to the degree of risk, but not less than once per year, except as described in 45 CFR 46.109(f).

### 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, the IRB must evaluate if the research continues to meet at 45 CFR 46.111 criteria in order for the IRB to approve research to continue. 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 IRBs 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 IRBs 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 consent document must occur during the scheduled continuing review of research by the IRB.

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

### 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?

Research approved prior to January 21, 2019 is subject of pre-2018 regulation requirements and will undergo continuing review in accordance with regulations of 45 CFR 110 (b).

In addition, post January 21, 2019 the IRB will review at least annually and apply expedited review procedures for the following type of non-FDA regulated research approved under expedited categories in accordance with 45 CFR 46.110:

* Research approved under any expedited category and include vulnerable populations
* Research involving deception
* Studies with multiple phases and not all phases are available/developed at the time of initial review
* Interventional studies with the FDA approved drug or device initially approved via expedited review
* Studies that involve sensitive information that present increase risk to employability, insurability, social stigmatization, criminal and civil liability
* Interventional studies previously reviewed by the convened IRB and the research involves no greater than minimal risk and no additional risks have been identified.
* The research previously approved by the convened IRB where no subjects have been enrolled and no additional risks have been identified

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.

### WHEN IS CONTINUING REVIEW IS NOT REQUIRED?

As of January 21, 2019 continuing review of research is not required in the following circumstances in accordance with 45 CFR 46 109(f):

1. Research eligible for expedited review in accordance 45 CFR 45.110 (except when criteria in section above applies)

2. Research that fall under the following exempt categories and requiring limited IRB review: category 2(iii), 3(i)(C),,7 or 8;

3. Research that has progressed to the point of Data analysis, including either analysis of identifiable private information or identifiable biospecimen or accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

### HOW IS THE CONTINUING REVIEW DATE DETERMINED?

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.

The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval when continuing review is requiredtherefore, continuing review and re-approval of research requiring continuing review 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.