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To: Investigators and Members of Investigative Teams

Date: April 23, 2010 (revised April 26, 2012)

Subject: CHOP IRB Review Process of External Adverse Event Reports

Procedure for External SAE Reports

Effective May 1, 2010 the IRB at The Children's Hospital of Philadelphia will no longer review individual external adverse event reports from multicenter trials submitted by pharmaceutical sponsors and cooperative groups. The IRB will only review those reports that meet the criteria for an unanticipated problem. Investigators and study teams should place all other reports in their study binders but need not report these to the IRB.

An *unanticipated problem* involving risks to subjects or others means any incident, experience or outcome that is:

- unexpected (in terms of the nature, severity or frequency) given (a) the description of the likely harms in the protocol, the consent form or the other materials submitted to the IRB and (b) the characteristics of the subject population;
- related to a subject's participation in the research; and
- suggests that the research places subjects or others at greater risk of harm - physical, psychological, economic or social harms - than was previously known or recognized.

Reports that suggest that the research places subjects or others at greater risk of harm should be accompanied by an Action Plan/amendment to mitigate the newly identified risk. The Action Plan/amendment might include any or all of the following: a modification to the protocol, consent form, or the study procedures or a notification of current or former study participants.

Rationale

The IRB reviews hundreds of external reports each month that add little to the understanding of risk to subjects. The preparation, review and correspondence related to these reports wastes investigative team and IRB time and resources.

The federal regulations and the OHRP, FDA, and NIH Guidance documents suggest that it is neither useful nor necessary under the HHS regulations at 45 CFR part 46 and 21 CFR 312 to distribute reports of individual adverse event reports or IND safety reports occurring in subjects enrolled in multicenter studies to investigators or IRBs at all institutions conducting the research.

Therefore, the IRB will only review single reports of external adverse events that meet the following conditions:

- The reported event is an unanticipated problems involving risks to subjects or others;

- The report is accompanied by an analysis prepared by the sponsor or cooperative group detailing how the reported event differs from prior reports; and
- The report is accompanied by a proposed Action Plan/amendment written by either the sponsor or the CHOP Principal Investigator detailing the proposed changes to either the protocol, the consent form, the notification of current/former participants, or the study procedures.

All other external reports or IND safety reports that are forwarded by the study sponsor should be simply filed in the site study files. A copy of this memo should be kept in the study file in the event a disagreement arises with sponsor's study monitor.

What types of safety reports should the investigator continue to submit to the IRB?

The IRB will continue to review the following materials:

- Data and Safety Monitoring Board (DSMB) reports.
- Study progress reports submitted at the time of continuing review. External SAE reports or other unanticipated problems that do not meet the criteria for prompt reporting may be briefly summarized in the progress reports.
- Unanticipated device effects, which are required to be distributed under 812.150 (b)(1) to the FDA and all reviewing IRBs.

What about internal reports of unanticipated problems from single-center studies conducted at CHOP?

The IRB will continue to review individual internal adverse event reports submitted by CHOP investigators for single center studies provided that the event meets the definition of an unanticipated problem involving risks to subjects or others.

Resources

IRB SOP 802: Unanticipated Problems Involving Risks to Subjects or Others
https://intranet.research.chop.edu/download/attachments/2097312/IRBSOP408.pdf?version=1&modificationDate=1233855115833

CHOP IRB Website: A page devoted to Reportable Events is available that includes discussion of SAE reports, protocol deviations and other unanticipated problems. The page also contains an algorithm for determining which internal events require reporting to the IRB.
https://intranet.research.chop.edu/display/cmtirb/Reportable+Events

OHRP Guidance: "OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events" dated January 15, 2007.
http://www.hhs.gov/ohrp/policy/AdvEvntGuid.pdf

FDA Draft Guidance: "Guidance for Clinical Investigators, Sponsors, and IRBs: Adverse Event Reporting Improving Human Subject Protection. Draft Guidance"
http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm127346.pdf