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MEMORANDUM

To: IRBs and Institutions enrolled in the CIRB Initiative; Clinical Trials Monitoring Branch, CTEP; Cooperative Group Chairs, Audit Coordinators, and Administrators

From: John Horigan, MA, CIP
CIRB Administrator 

Date: April 1, 2010

Subject: **Change in CIRB Review Process of Adverse Event Reports for Phase 3 Clinical Trials**

Effective immediately, the adult and pediatric CIRBs will no longer review individual adverse event reports related to Phase 3 CTEP-sponsored multicenter trials that are submitted by Cooperative Groups to the CIRBs and investigators. The pediatric CIRB will continue to review individual adverse event reports submitted by COG to the pediatric CIRB that are related to Phase 2 and Pilot CTEP-sponsored multicenter trials.

The adult and pediatric CIRBs have historically reviewed all individual adverse event reports submitted by Cooperative Groups to the CIRBs and investigators participating in CTEP-sponsored multicenter trials. Existing OHRP, FDA, and NIH Guidances suggest that it is neither useful nor necessary under the HHS regulations at 45 CFR part 46 and 21 CFR 312 for reports of individual adverse events occurring in subjects enrolled in multicenter studies to be distributed routinely to investigators or IRBs at all institutions conducting the research. The Guidances recommend that individual adverse event reports be submitted for review and analysis to a monitoring entity [e.g., the research sponsor, coordinating or statistical center, or a Data and Safety Monitoring Board (DSMB)] so a contextual view of adverse events occurring on a specific trial is obtained. Only those events that meet the criteria for an unanticipated problem should be reported to investigators and IRBs. Since CTEP-sponsored Phase 3 trials are mandated to have a study-specific DSMB, the adult and pediatric CIRBs are changing their current adverse event report review process pertaining to Phase 3 trials to reflect the review recommendations contained in the above cited Guidances.

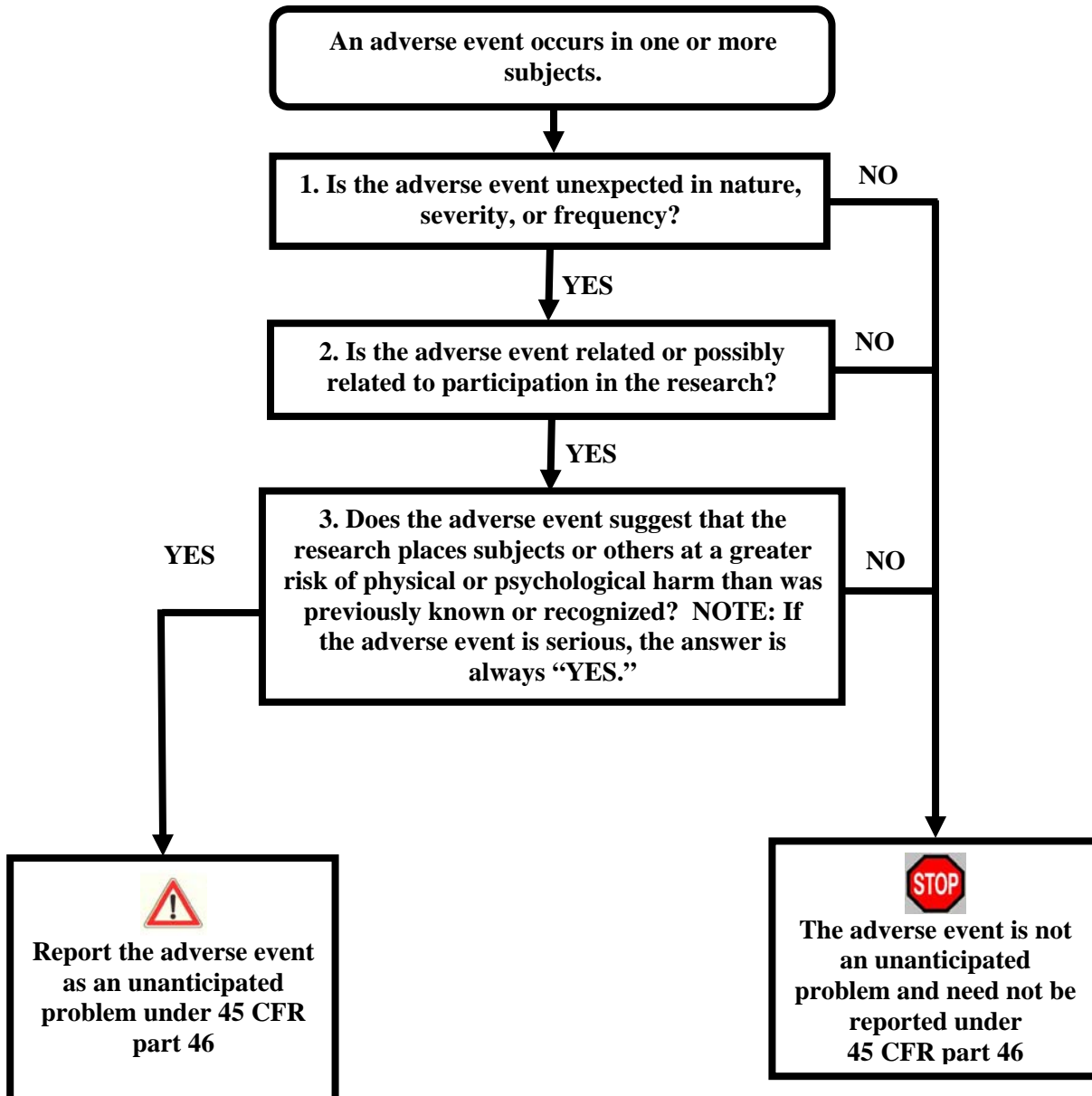
The adult and pediatric CIRBs will review the Data and Safety Monitoring Board (DSMB) report and the study report at time of continuing review. Study Chairs will be required to provide the most current DSMB report and study report with the CIRB Continuing Review Application. CIRB review of each study for continuation will be dependent upon receipt of the DSMB report and study report.

In addition to review of DSMB reports, the adult and pediatric CIRBs will review any unanticipated problems identified and reported to the CIRB by CTEP or the Cooperative Groups. The CIRBs will also review Action Letters distributed by a sponsor as well as any adverse event report resulting in a change in the protocol or informed consent document. During its review, the CIRB will determine if the Action Letter or adverse event report resulting in an amendment meet the criteria for an unanticipated problem. If so, the CIRB will report the unanticipated problem per the Federal regulations.



Please find included a copy of the OHRP algorithm for determining whether an adverse event is an unanticipated problem. This algorithm has been excerpted from the “OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events” dated January 15, 2007. The URL for each Guidance is attached to this memo for ease of your review.

OHRP Algorithm for Determining Whether an Adverse Event is an Unanticipated Problem





OHRP, FDA, and NIH Guidance URLs

OHRP: “Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events” (January 15, 2007).

<http://www.hhs.gov/ohrp/policy/AdvEvtGuid.htm>

FDA: “Adverse Event Reporting to IRBs – Improving Human Subject Protection” (January 2009).

<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126572.pdf>

NIH: “Guidance on Reporting Adverse Events to Institutional Review Boards for NIH-Supported Multicenter Clinical Trials” (June 11, 1999).

<http://grants.nih.gov/grants/guide/notice-files/NOT99-107.html>