DUKE UNIVERSITY HEALTH SYSTEM
Human Research Protection Program

REPORTING IRB FINDINGS TO DUHS OFFICIALS AND FEDERAL REGULATORY AGENCIES

11/20/2023

Federal regulations (45 CFR 46.108(a)(4) and 21 CFR 56.108(b)) require that DUHS have written policies and procedures in place to ensure prompt reporting to the IRB, appropriate institutional officials, and the appropriate federal department or agency of:

(I) an unanticipated problem involving risks to subjects or others (UPIRTSO),
(II) a suspension or termination of IRB approval, and
(III) an instance of serious or continuing noncompliance with applicable federal regulations or the requirements or determinations of the IRB.

I. UPIRTSO

UPIRTSO determinations are made either by a convened IRB or, in the case of UPIRTSOs that present a minimal risk to subjects and others, by an IRB Chair or the Executive Director via expedited review.

UPIRTSO reports are prepared by the Executive Director or designee twice monthly in the format described in the attached Appendix A. The first monthly report contains the determinations of IRBs #1-4, and the second monthly report contains not only the determinations of IRBs #5-9 and 10 but also all UPIRTSOs reviewed by the expedited process for the entire month. UPIRTSO reports are provided to the Executive Director, Lead IRB Chair, Vice Dean for Scientific Integrity, Director for Sponsored Programs Assurance and Research Compliance (OARC), the Vice Dean for Clinical Research and the QA & Regulatory Compliance Associate.

The above UPIRTSO reports are also sent twice monthly to the Office for Human Research Protections (OHRP) and the US Food & Drug Administration (FDA), as applicable. A file of these external reports is maintained on the IRB shared drive.

II. Suspensions or Terminations of IRB Approval

The PI is immediately notified via email by the reviewing IRB Chair of a suspension or termination of a research study. In addition, such suspensions or terminations are immediately emailed to the Vice Dean for Scientific Integrity for presentation to the IO, with copy to the Executive Director, Lead IRB Chair, Clinical Research Unit (CRU) Medical Director for the study, the Director for

Sponsored Programs Assurance and Research Compliance (OARC), the Vice Dean for Clinical Research and, as necessary, University Counsel and Risk Management.

A letter is immediately prepared by the Executive Director or designee, with assistance from the relevant IRB Chair, and sent to OHRP and/or FDA as applicable. The letter will contain all known details of the event, corrective actions, risks to participants, effect on data integrity, and institutional actions, and will be signed by the IO. Follow-up correspondence to these agencies will be submitted as warranted.

III. Serious and/or Continuing Noncompliance

The PI of the relevant study is made aware of the convened IRB's recommendation via the outcome letter sent to the study team within 3 days post-meeting.

Recommendations of serious and/or continuing noncompliance, as made by the convened IRBs, are sent by the Executive Director or designee in the form of a letter to the Vice Dean for Scientific Integrity for presentation to the IO for final determination. The email containing this letter is copied to the Executive Director, IRB Lead Chair, Vice Dean for Clinical Research, and the Director for Sponsored Programs Assurance and Research Compliance (OARC).

If the IO concurs with the IRB's recommendation, the letter bearing the IO's signature is emailed directly from the IO's office to OHRP and/or FDA, as appropriate, with copy to the Executive Director or designee. Once the IO has made its decision, a notice of the IO determination will be sent to the PI, study coordinator, and regulatory coordinator. A record of the signed determination letter is maintained on the IRB's secure shared drive.

The template for a serious/continuing noncompliance letter is attached as Appendix B.

IV. Reporting to AAHRPP

The following occurrences will be reported to AAHRPP as soon as possible but generally within 48 hours after DUHS IRB becomes aware of: (i) Any negative actions by a government oversight office, including, but not limited to, OHRP Determination Letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated, FDA Restrictions placed on IRBs or Investigators, and corresponding compliance actions taken under non-US authorities related to human research protections. (ii) Any litigation, arbitration, or settlements initiated related to human research protections. (iii) Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding the HRPP.

APPENDIX A – UPIRTSO REPORT TEMPLATE

Institutional Review Board
Duke University Health System, Inc.
Unanticipated Problems Involving Risks to Subjects or Others (UPIRTSO)
[Date Range]

DUHS IRB#:
Study Title:
DUHS PI:
IND/IDE #:
IND/IDE Holder:
Enrollment:

Study Summary:

Event(s):

PI's Proposed Corrective Action(s):

Board Determinations:

Reported to:

NOTE: The following format is used in the second monthly UPIRTSO report only, for minimal risk UPIRTSOs reviewed by the expedited process:

The following UPIRTSO determinations were made by an IRB Chair/designee via the expedited review process during the period *[Date Range]*. These UPIRTSOs, as per DUHS IRB policy, were determined by the reviewer to involve no more than minimal risk to subjects. Unless otherwise noted, the corrective actions proposed by the PI were determined by the reviewer to be appropriate. UPIRTSOs determined by this process are reported to the convened IRB each month. None of the UPIRTSOs below were determined to constitute serious or continuing noncompliance.

DUHS IRB#:
Study Title:
DUHS PI:
IND/IDE #:
INDE/IDE Holder:

Event(s):

PI's Proposed Corrective Action(s):

Reported to:

APPENDIX B – SERIOUS/CONTINUING NONCOMPLIANCE LETTER TEMPLATE

Date

Division of Scientific Investigations (RD-45)
Office of Compliance
Center for Drug Evaluation and Research
White Oak Campus
10903 New Hampshire Avenue, Bldg 51, Rm 5341
Silver Spring, MD 20993

RE: Determination Related to an FDA-Regulated Research Study at Duke

Dear Sir/Madam:

The purpose of this letter is to advise you, in accordance with the reporting requirements of 21 CFR 56.108(b)(2), of the recommendation by the Duke University Health System Institutional Review Board (DUHS IRB) of (**continuing or serious) noncompliance** related to an FDA-regulated research study at Duke. After reviewing the supporting documentation, I have concurred with this recommendation in my role as Institutional Official for DUHS.

My determination of [continuing/serious] noncompliance results from the DUHS IRB's review of the following protocol:

DUHS IRB #:
Title:
Funding Source:
DUHS PI:
IND/IDE Number:
IND/IDE Holder:
Number Enrolled:

I. Study Summary

II. Event(s)

III. PI's Proposed Corrective Actions

IV. Board Determinations

V. Institutional Actions

After careful consideration of the supporting documentation, I have concurred with the DUHS IRB's recommendation of [continuing/serious] noncompliance.

The DUHS IRB and the entire Human Research Protections Program at Duke are dedicated to upholding the highest ethical and scientific standards in the conduct of research with human participants.

Please do not hesitate to contact Sharon Ellison, Executive Director, DUHS IRB, at sharon.ellison@duke.edu if you wish to discuss this study and my determination further.

Thank you.

Sincerely,

Mary E. Klotman, MD
DUHS Institutional Official
Vice Chancellor and for Health Affairs
Dean, Duke University School of Medicine

cc: DUHS IRB Lead Chair
Vice Dean for Scientific Integrity
Duke Office of Audit, Risk and Compliance
Vice Dean for Clinical Research