COLUMBIA UNIVERSITY INSTITUTIONAL REVIEW BOARD GUIDANCE

WITHDRAWAL OF SUBJECTS FROM FDA-REGULATED STUDIES

I. SCOPE:

This Guidance applies to all research involving human subjects that is regulated by the Food and Drug Administration (FDA), and generally applies to all clinical trials involving investigational drugs, biologics, or devices. This guidance provides insights on how to best handle subjects who voluntarily drop-out from a clinical trial or are withdrawn from the study by the clinical investigator.

II. EFFECTIVE DATE: September 10, 2012, revised April 4, 2018.

To the extent provided herein, this Guidance provides additional guidance to the Columbia University "Informed Consent Policy".

III. BACKGROUND:

The FDA issued "Guidance for Sponsors, Clinical Investigators, and IRBs – Data Retention When Subjects Withdraw from FDA-Regulated Clinical Trials" in October 2008. The guidance provides clarifications regarding FDA's longstanding policy that data that has already been collected from subjects must be retained in the study data for the given clinical trial even if the subject voluntarily drops-out of the study. Additionally, the FDA guidance provides standards for ensuring that appropriate informed consent has been, or will be, obtained for any follow-up procedures or monitoring in which a subject may agree to participate.

IV. GUIDANCE

In an effort to ensure the ethical conduct of human subjects research, investigators must respect a participant's request to stop or reduce his/her participation in a research study. Often such a request from a participant may arise due to inconvenience or challenges to the participant of continuing study-related activities or therapy. Likewise, an investigator may decide to remove a subject from a study either because the subject is not following instructions, to ensure compliance with the study protocol, or the subject may have experienced toxicity or adverse events to the study drug or therapy.

For whatever reason that a subject or an investigator decides that a subject's participation should cease or be reduced, the investigator should make efforts to conduct an exit visit to assess the safety and well-being of the subject. Such an exit visit should include a physical exam and all safety monitoring procedures that were required by the study protocol for the exit visit. The exit visit should be performed as soon as possible after the withdrawal of any investigational treatment or intervention.

When subjects request to stop or reduce their participation in a study, an investigator often will ask the subject to continue participation for at least some of the study procedures. The FDA guidance states:

> "An investigator may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject would distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the subject's information.
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> If a subject withdraws from the interventional portion of the study, but agrees to continued follow-up of associated clinical outcome information as described in the previous bullet, the investigator must obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). In accordance with FDA regulations, IRB approval of informed consent documents would be required (21 CFR 50.25, 56.109(b), 312.60, 312.66, 812.100).
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> According to FDA regulations, when a subject withdraws from a study, the data collected on the subject to the point of withdrawal remains part of the study database and may not be removed.
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> If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the investigator must not access for purposes related to the study the subject's medical record or other confidential records requiring the subject's consent. However, an investigator may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status."

The handling of such requests by the investigators should be in a manner that is respectful and considerate of the subject's requests while also balancing the subject's safety and the scientific needs of the study. An investigator can enhance the ethical conduct of the study by encouraging the subject to continue with procedures that will facilitate their safety while eliminating some or all of the study procedures that a subject is no longer willing to have performed. The investigator should not put undue influence or coercion to keep a subject in a study.

In addition to FDA guidance noted above which clarifies data collected from the subject to the point of withdrawal should remain as part of the study database, the IRB will review the consent document for all FDA-regulated research to ensure that the consent document does not give the subject the option of having data removed upon withdrawal.