

Guidance for the Submission of Investigator's Drug Brochures (IDBs) April 25, 2009

Background

In order to approve research studies under the Common Rule (45 CFR 46) or FDA regulations (21 CFR 56), an IRB must receive sufficient information about the effects of any drug under study to assess whether the risks to subjects are reasonable in relation to anticipated benefits and adequately minimized. For studies conducted under an investigational new drug (IND) application FDA guidance notes that an investigator's drug brochure (IDB) is usually required by the FDA (21 CFR 312.23(a)(5) and 312.55). In addition, FDA guidance states that even though 21 CFR 56 does not mention the investigator's brochure by name, much of the information contained in such brochures is "clearly required to be reviewed by the IRB" (FDA Information Sheets at <http://www.fda.gov/oc/ohrt/irbs/faqs.html>). The FDA provides flexibility to IRBs regarding when IDBs are required to be submitted, the format for submission, and how the IRB assesses the brochures.

The Health Sciences IRB has decided to change its submission and review process for revised IDBs. Prior to this change, research teams were required to submit IDBs to the Health Sciences IRB as they are received via a *Revised Investigator's Drug Brochure* form whether or not the documents contained revisions that affect the study's risks/benefit ratio or represented new information that should be conveyed to subjects. This submission requirement led to many challenges for both study teams and the IRB, especially when study sponsors did not provide IDBs in a timely manner and the information contained in the IDB already had been submitted to the IRB through other channels (e.g., action letters, changes of protocol).

Submission and review process for revised IDBs

The revised process adopted by the Health Sciences IRB will be more consistent with adverse event reporting guidelines for FDA-regulated trials involving drugs. Using the adverse event reporting model, if a study team was required to submit an IDB at the time of the initial consideration of the research study, updated IDBs would be required to be submitted as follows:

- 1) **At the time of continuing review** if the IDBs do not contain revisions that (1) affect the risk/benefit ratio of the study (e.g., result in a change to the protocol); (2) affect alternatives to study participation for subjects; or (3) represent new information that should be provided to subjects. If the information contained in a revised IDB has already been submitted to the IRB for review (e.g., as a change of protocol), the IDB can then be submitted at the time of continuing review as well.

In these cases, research teams will be required to append a *Revised Investigator's Drug Brochure* form to the *Continuing Review of Previously Approved Research* form and provide a brief summary of the revised information in all IDBs that have been received either since the initial review or last

continuing review, whichever was most recent, and have not been submitted to the IRB previously. As part of this form, study teams will be asked to explain why the IDBs that were assessed did not meet any of the 3 criteria noted above that would require submission prior to continuing review. Only 1 copy of each IDB that has not been previously is required to be submitted at continuing review.

- 2) **Within 60 days of receipt by the study team** if the IDBs contain revisions that (1) affect the risk/benefit ratio of the study (e.g., result in a change to the protocol); (2) affect alternatives to study participation for subjects; or (3) represent new information that should be provided to subjects.

When an IDB meets any of these 3 criteria, research teams should append a *Revised Investigator's Drug Brochure* form to the *Application for Change to Previously Approved Research* form that describes revisions to consent documents or the protocol or the creation of documents that provide new information to subjects (e.g., letters to participants). In addition, research teams should submit any IDBs that had not been submitted previously to the IRB at that point. For example, a research team may have submitted version 1 of an IDB at the time of initial review. Version 2 of the IDB is issued within 2 months of the study's approval, but is not submitted to the IRB yet because it is judged to not 1) affect the risk/benefit ratio of the study (e.g., result in a change to the protocol); (2) affect alternatives to study participation for subjects; or (3) represent new information that should be provided to subjects. However, eight months after the study's approval, version 3 of the IDB is issued, which contains new risk information the research team has not received via other routes and the research team believes the information should be included in the consent form. Both Versions 2 and 3 would be described in the *Revised Investigator's Drug Brochure* form appended to the *Application for Change to Previously Approved Research* form. Under this new approach, it is possible that no IDBs subsequent to the initial review are submitted to the IRB until continuing review. If an IDB has been submitted to the IRB for review prior to the continuing review of the study, the document does not need to be resubmitted at continuing review.