

DFCI Institutional Review Board Policy on Receipt and Review of IND/IDE Safety Reports

IND/IDE Safety Reports from outside sponsors or institutions seldom contain sufficient information to allow the Principal Investigator or the IRB to make a meaningful judgment about whether or not the reported event that has occurred at a site outside of the DF/HCC has implications for the conduct of the study. Until now, the DFCI IRB has been receiving all IND/IDE safety report submissions regardless of the type of information contained in the report.

The DFCI IRB is instituting a new policy regarding the receipt and review of IND/IDE safety reports. This new policy is in line with guidance issued by the Office for Human Research Protections in September 2003 and by the Food and Drug Administration in January of 2009.

As of March 1, 2009, the Dana-Farber Cancer Institute (DFCI) Institutional Review Board (IRB) will not accept IND/IDE Safety Reports reporting events that take place outside of the DF/HCC by outside sponsors unless the event is:

1. Serious or Life-Threatening; **and**
2. Unexpected; **and**
3. Related to the Research Intervention; **and**
4. **Has an implication for the conduct of the study you are conducting using this study intervention**
(Example: the new risk changes the original risk benefit ratio of the study approved by the IRB. This would also apply to informing subjects previously treated with the agent of newly identified potentially serious long-term risks.)

Responsibility of Principal Investigator

It is the responsibility of the Principal Investigator to review all IND/IDE safety reports provided by an outside sponsor (or themselves if they are the sponsor) **within 60 days of receipt** and determine that indeed the four criteria above DO NOT APPLY.

Any sponsor correspondence requiring immediate action as a result of an adverse event/unanticipated problem and requiring modifications to a protocol, informed consent document or investigator's brochure (e.g. NCI Action letters) must be submitted as an amendment to the OHRS **within 10 days of receipt**.

IND/IDE meets the criteria above

If the IND/IDE safety report **does meet** all of the criteria noted above, the Principal Investigator must submit the IND/IDE safety report to the IRB, through OHRS Submit, via the amendment form **within 90 days from original date of receipt** including any applicable changes to the protocol and/or consent form.

IND/IDEs that are not submitted

The continuing review form will include a new requirement that Principal Investigators attest to the review of all IND/IDE safety reports that have been issued during the year but not submitted to the IRB because they do not meet the criteria above.

Information for Sponsors

The Letter to Sponsors that is available on the OHRS website now includes a paragraph stating that the DFCI IRB will not accept IND/IDE safety reports unless they meet the four criteria noted above. This can be provided to Sponsors who require submission of IND/IDE safety reports to the institution's IRB and need some acknowledgement that the DFCI IRB does not accept these submissions.

FDA Definitions 21 CFR 312.32(a)

Associated with the use of the drug: There is a reasonable possibility that the experience may have been caused by the drug.

Disability: A substantial disruption of a person's ability to conduct normal life functions.

Life-threatening adverse drug experience: Any adverse drug experience that places the patient or subject, in the view of the investigator, at immediate risk of death from the reaction as it occurred, i.e., it does not include a reaction that, had it occurred in a more severe form, might have caused death.

Serious adverse drug experience: Any adverse drug experience occurring at any dose that results in any of the following outcomes: Death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

Unexpected adverse drug experience: Any adverse drug experience, the specificity or severity of which is not consistent with the current investigator brochure; or, if an investigator brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the investigator brochure only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the investigator brochure only listed cerebral vascular accidents. "Unexpected," as used in this definition, refers to an adverse drug experience that has not been previously observed (e.g., included in the investigator brochure) rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product.

Please contact OHRS if you have further questions.