DF/HCC and DFCI IRB 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 a reported event that has occurred at a site outside of the DF/HCC has implications for the conduct of the study.

The following describes the DF/HCC policy and Dana-Farber Cancer Institute (DFCI) Institutional Review Board (IRB) policy regarding the receipt, review and reporting of IND/IDE safety reports. This policy is in line with guidance issued by the Office for Human Research Protections in January 2007 and by the Food and Drug Administration in January 2009.

DF/HCC Policy for Receipt and Review of IND/IDE Safety Reports by the DF/HCC Overall Principal Investigators - Effective December 1, 2017:

DF/HCC policy is based on the expectation that external study sponsors will actively notify DF/HCC Investigators of unanticipated problems and important safety information that has implications for the conduct of the research or involves new risks to subjects. Sponsors are expected to bring such information to the attention of DF/HCC investigators and not simply post to Industry, CRO, or third-party web portals. Additionally, sponsors are required to provide sufficient information about any individual event to support a substantive review by investigators and the IRB.

For ALL DF/HCC Investigator-Sponsored Trials: It is the responsibility of any DF/HCC Investigator holding a study IND and acting as Study Sponsor to review all IND/IDE safety reports **within 60 days of receipt**, determine whether the four DFCI IRB criteria for reporting apply, and act accordingly.

For Externally Sponsored Pilot, Phase I and I/II Studies: It is the responsibility of the DF/HCC Overall PI to review all IND/IDE safety reports provided by an external sponsor **within 60 days of receipt,** determine whether the four DFCI IRB criteria for reporting below apply, and act accordingly.

For Externally Sponsored Phase II, II/III, III and IV Studies: Per Federal regulations (21 CFR 312.32, 21 CFR 312.55, 21 CFR 812.46, 21 CFR 812.150)**,** external sponsors must actively notify the DF/HCC Overall PI of events that meet the definition of an unanticipated problem involving risks to subjects or others that require a change to the research or informed consent document. Once notified by the sponsor, it is the responsibility of the DF/HCC Overall PI to review all events determined to be an unanticipated problem (as indicated by the sponsor) **within 60 days of receipt**, determine whether the four DFCI IRB criteria for reporting below apply, and act accordingly.

DFCI IRB Reporting Policy - Effective March 1, 2009:

The DFCI IRB will not accept IND/IDE Safety Reports reporting events that take place outside of the DF/HCC by outside sponsors unless the event meets all four (4)of the criteria listed below:

1. Serious or Life-Threatening; **and**
2. Unexpected; **and**

3. At least possibly related to the Research Intervention; **and**
4. **Has an implication for the conduct of the study requiring a change to the research**. (Example: a 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.)

Note: 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 DFCI IRB **within 10 days of receipt**.

IND/IDE safety report **meets** the DFCI IRB criteria for reporting:
The DF/HCC Overall PI must submit the IND/IDE safety report to the IRB as an amendment **within 90 days from original date of receipt** including any applicable changes to the research. OHRS will not accept any other type of submission.

For DF/HCC Investigator-Sponsored trials, the Sponsor-Investigator must also distribute the IND/IDE report, along with their assessment of the above criteria, to all participating DF/HCC Site Responsible Investigators and non-DF/HCC site Principal Investigators.

IND/IDE safety report **does not meet** the DFCI IRB criteria for reporting:
If the safety report does not meet all four criteria above, it should not be submitted to the IRB. The continuing review form includes a 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.

Receipt of IND/IDE safety reports prior to submission of a new protocol
If a Principal Investigator receives IND/IDE safety reports prior to submitting a new protocol application to OHRS, the investigator should review the IND/IDE safety report(s) as described above. If the safety report(s) meets the criteria described above, it should be submitted along with the New Project Application. Any IND/IDE safety reports identified as meeting the DFCI IRB reporting criteria AFTER the new protocol has been submitted must be submitted to OHRS as an amendment.

Note: Review of IND/IDE safety reports may occur after 90 days of receipt as long as the Principal Investigator reviews the received IND/IDE safety reports prior to submission of the new protocol application to OHRS.

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

Questions:
Questions about this policy can be emailed to the Adverse Event / Other Event Team at: OHRSEvent_Reporting@dfci.harvard.edu or please call to the OHRS main number at **(617) 632-3029**.