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Timetable for the Submission of Required Reports to the IND Application/FDA

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Revision History:
Version1: June 9, 2014
Version2: August 27, 2015

IND Safety Reports

Submission	Timing	Details
A. Serious and unexpected, suspected adverse reactions to the investigational drug or study treatment(s)	The FDA must be informed as soon as possible, but ***no later than 15 calendar days*** after the Sponsor of the IND application receives the respective information.	The serious and unexpected, suspected adverse reaction must be reported to the FDA using a Form FDA 3500A. Corresponding changes, if applicable, to the clinical studies being conducted under the IND should be submitted as Protocol Amendments. All reviewing IRBs must also be notified of serious and unexpected, suspected adverse reactions in accordance with the respective policies and procedures of the IRB. All Investigators (i.e., study site principal investigators) must also be promptly notified of serious and unexpected, suspected adverse reactions.
B. Unexpected life-threatening or fatal, suspected adverse reactions associated with the use of the investigational drug or study treatment(s)	The FDA must be informed as soon as possible, but ***no later than 7 calendar days*** after the Sponsor of the IND application receives the respective information.	The unexpected, life-threatening or fatal, suspected adverse reaction must be reported to the FDA using a Form FDA 3500A. Corresponding changes, if applicable, to the clinical studies being conducted under the IND should be submitted as Protocol Amendments. All reviewing IRBs must also be notified of unexpected, life-threatening or fatal, suspected adverse reactions in accordance with the respective policies and procedures of the IRB. All Investigators (i.e., study site principal investigators) must also be promptly notified of unexpected life-threatening or fatal, suspected adverse reactions.
C. Findings from other human studies (e.g., epidemiological studies, pooled analysis of multiple studies, or other clinical studies) that suggest a	The FDA must be informed as soon as possible, but ***no later than 15 calendar days*** after the Sponsor of the IND	Written reports of new significant risk findings from other clinical studies should be submitted to the FDA/IND application as a Safety Report incorporating a narrative format. Corresponding changes, if applicable, to the clinical studies being conducted under the IND should be submitted as Protocol Amendments.

previously unspecified (i.e., in the investigator's brochure or clinical protocol) significant risk to humans receiving the investigational drug.	application determines that the information qualifies for reporting.	All reviewing IRBs must also be promptly notified of findings from other clinical studies that suggest a new significant risk to research subjects. Current and potential research subjects must be informed of such new information which may affect the risk-to-benefit ratio of their study participation.
D. Findings from animal studies (e.g., toxicology) or in vitro testing (e.g., mutagenicity, teratogenicity) that suggest a previously unspecified (i.e., in the investigator's brochure or protocol) significant risk to humans receiving the investigational drug.	The FDA must be informed as soon as possible, but ***no later than 15 calendar days*** after the Sponsor of the IND application determines that the information qualifies for reporting.	Written reports of new significant risk findings from animal or *in vitro* studies should be submitted to the FDA/IND application as an Information Amendment incorporating a narrative format. Corresponding changes, if applicable, to the clinical studies being conducted under the IND should be submitted as Protocol Amendments. All reviewing IRBs must also be promptly notified of findings from animal or *in vitro* studies that suggest a new significant risk to research subjects. Current and potential research subjects must be informed of such new information which may affect the risk-to-benefit ratio of their study participation.
E. Increased rate of occurrence of serious, suspected adverse reactions.	The FDA must be informed as soon as possible, but ***no later than 15 calendar days*** after the Sponsor of the IND application determines that the information qualifies for reporting.	Written reports addressing an observed increase rate of serious, suspected adverse reactions should be submitted to the FDA/IND application as a Safety Report incorporating a narrative format. Corresponding changes to the clinical studies being conducted under the IND should be submitted as Protocol Amendments. All reviewing IRBs must also be promptly notified of an observed increase rate of serious, suspected adverse reactions. Current and potential research subjects must be informed of such new information which may affect the risk-to-benefit ratio of their study participation.

IND Annual Report

Submission	Timing	Details
IND Annual Report	The Sponsor of the IND application must submit annually (i.e., within 60 days of the anniversary of the date that the IND was initially accepted by the FDA) an Annual Report to the IND application/FDA.	The Annual Report must include a written summary of the status of all clinical studies being conducted under the IND application. Written summaries of the status of the clinical studies must also be submitted to the responsible IRB on an annual basis, or more frequently if required by the responsible IRB.

IND Withdrawal or Discontinuation Notice

Submission	Timing	Details
A. Withdrawal of the IND application upon completion of the clinical study (studies) of the investigational drug	At the time that all clinical studies of the investigational drug have been completed, and no future studies are planned, the Sponsor of the IND application should notify the FDA, in writing, that the IND is being withdrawn or terminated.	A final report of the outcome of all clinical studies conducted under the IND application should be submitted to the IND application/FDA. All current participating Investigators and reviewing IRBs must be notified of the withdrawal or discontinuance of the IND, and should be provided a copy of the final report submitted to the FDA. All investigational drug supplies should be returned to the Sponsor or disposed of in accordance with the instructions of the Sponsor.
B. Withdrawal of the IND application due to <u>safety issues or concerns</u>	The Sponsor of the IND application must discontinue the respective clinical study (studies) of the investigational	In addition to notifying the IND application/FDA, all (current and past) participating investigators, and all reviewing IRBs must be <u>promptly</u> notified, in writing, of discontinuation of the clinical study (studies) of the investigational drug due to safety issues or concerns and the specific circumstances leading to this

	drug as soon as possible, and in no event later than 5 days after making the determination that the clinical study (studies) should be discontinued due to safety issues or concerns**.** If applicable, the Sponsor must promptly notify the FDA, in writing, of the corresponding withdrawal of the IND application.	decision. If applicable (i.e., no additional clinical studies of the investigational drug will remain ongoing or are planned), all investigational drug supplies should be returned to the Sponsor or disposed of in accordance with the instructions of the Sponsor.

Protocol Amendments

Submission	Timing	Details
A. New Clinical Protocol	The Sponsor of the IND application must submit a Protocol Amendment to the IND application/FDA prior to implementing any new clinical protocol involving the use or evaluation of the investigational drug.	The new clinical protocol may be implemented provided that two conditions are met: (1) the Protocol Amendment corresponding to the new clinical protocol has been submitted to the IND application/ FDA; and (2) the new clinical protocol has been reviewed and approved by an IRB that functions in accordance with the FDA regulations at 21 CFR Part 50 and 21 CFR Part 56.

B. Changes to a previously submitted clinical protocol	The Sponsor of the IND application must submit a Protocol Amendment to the IND application for any proposed revision to a Phase I protocol that significant affects the safety of the research subjects; or to a Phase 2 or 3 protocol that significantly affects the safety of the research subjects, the scope of the investigation, or the scientific quality of the study.	The proposed revisions to the protocol may be implemented provided that two conditions are met: (1) the Protocol Amendment corresponding to the revised protocol has been submitted to the IND application/FDA; and (2) the proposed revisions to the protocol have been reviewed and approved by the IRB that has responsibility for oversight of the initial protocol. Note: A protocol deviation directed at eliminating an apparent *immediate hazard to a research subject or group of subjects* may be implemented immediately provided that the reviewing IRB is so notified. The respective protocol deviation should be addressed in the next Annual Report to the IND application. If the protocol deviation will be incorporated as a permanent change (i.e., revision) to the protocol, a respective Protocol Amendment must be submitted prospectively to the IND application/FDA and the revision to the protocol must be approved prospectively by the responsible IRB.
C. New Investigator (i.e., new study site principal investigator)	The Sponsor of the IND application must submit, within 30 days, a Protocol Amendment to address the involvement of a new Investigator/study site in the conduct of clinical studies incorporated under the IND application.	Implementation of the protocol under the direction of the new Investigator may proceed provided that two conditions are met: (1) the Protocol Amendment corresponding to the new Investigator/study site has been submitted to the IND application/FDA; and (2) conduct of protocol by the new Investigator/study site has been approved by an IRB that has responsibility for this Investigator/study site.

Information Amendments

Submission	Timing	Details
Information Amendments	The Sponsor of the IND Application should submit Information Amendments to the IND application as necessary to keep the IND current but, to the extent feasible, not more than every 30 days.	Information Amendments to the IND application should address new, essential information (e.g., changes in the manufacture of the investigational drug, technical information) pertaining to the investigational drug, which does not fall within the scope of a Protocol Amendment, IND Safety Report or the IND Annual Report.

For specific questions at VCU/VCUHS contact the Clinical Research Compliance Officer:

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