Withdrawal of IND Application for an Investigational Drug:  IND Withdrawal Guidance and Template for Investigational Drug Products

ICTR Navigator
October 31, 2012
Version 1.0
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2.0 Abbreviations

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<tr>
<td>IND</td>
<td>Investigational New Drug</td>
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<tr>
<td>CFR</td>
<td>Code of Federal Regulations</td>
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<tr>
<td>FDA</td>
<td>U.S. Food and Drug Administration</td>
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<tr>
<td>CDER</td>
<td>Center for Drug Evaluation and Research</td>
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<tr>
<td>CBER</td>
<td>Center for Biologics Evaluation and Research</td>
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3.0 FDA Websites

Within this document, there are a number of links to various FDA forms, regulations, and/or guidance documents. The list below contains additional useful FDA websites.

**FDA Title 21 Part 312.38 Withdrawal of an IND:**

**FDA Title 21 Regulations Search Engine (e.g., IND regulations Part 312):**

**FDA CBER SOPP 8110: Submission of Paper Regulatory Applications to CBER**
- [http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/ucm079467.htm](http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/ucm079467.htm)

**FDA CDER binding guidance information entitled FDA IND, NDA, ANDA, or Drug Master File Binders**
- [http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm](http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm)
4.0 Introduction

The enclosed information is intended to provide an overview of the process for requesting withdrawal of an Investigational New Drug (IND) as per the requirements set forth in 21 CRF 312.38. This document is designed to be used for an active IND for a drug product that is under the review of the FDA Center for Drug Evaluation Research (CDER) or Center for Biologics Evaluation and Research (CBER).

4.1 Points to Consider

4.1.1 Inactive INDs

An inactive IND is subject to no activity, but may be reactivated (21 CFR 312.45) at request of sponsor or by FDA if certain conditions are met. FDA may inactivate an IND if kept on hold for more than 1 year. Once inactive for 5 years, FDA may terminate an IND.

FDA may inactivate an IND if no subjects are entered into clinical studies for 2 years or more. Sponsor-investigators of inactive INDs are not required to submit an annual report to FDA; however, the IND still in effect for purposes of public disclosure of information & data under 21 CFR 312.130.

In general, inactive INDs cannot be cross-referenced. Reactivation may occur with submission of a new protocol, updated manufacturing information, etc. Reactivation of an inactive IND is subject to 30 day review clock.

Sponsor-investigators of gene therapy trials should inactivate rather than withdraw their INDs based on requirements for long-term patient follow up.

- Retroviral INDs have life-long patient follow-up.
- Adenoviral INDs have 15 year patient follow-up.

4.1.2 Withdrawn INDs

If withdrawing an IND, all trials must be ended and these are considered ‘dead files’ that cannot be resuscitated (i.e. an entirely new IND submission would be required.) Additionally, withdrawn INDs cannot be cross-referenced.

Finally, FDA does not recommend that sponsors submit information to withdrawn files because submissions to withdrawn INDs are not tracked by the Document Control Center or Regulatory Project Managers.

4.1.2.1 Final Reports

Although not formally noted in the regulations, on occasion the FDA may ask a sponsor-investigator to submit any outstanding information (including publications) not already included in annual reports or other IND submissions before they withdraw the IND. Otherwise, the Code of Federal Regulations does not require submission of final clinical study reports to FDA.
4.2 Guidance-Template General Information

The enclosed template guidance is a suggested format based on federal regulations, and guidance documents. Within the template are references to applicable FDA regulations, web addresses to FDA guidance documents, comments/instructions, web addresses to FDA forms, and suggested formatting and/or language. These instructions outline what may need to be included or inserted into a particular section and any special considerations.

4.3 Submission binding, labeling, and mailing addresses for CDER and CBER

One original and two photocopies of IND withdrawal request must be sent with the submission.

4.3.1 Labels

Binders should be identified with the following label:

WITHDRAWAL OF IND
IND. NO._____
SPONSOR NAME
NAME OF INVESTIGATIONAL AGENT

4.3.2 Binding

1. FDA CDER Guidance Recommendations:

http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm

2. FDA CBER Guidance Recommendations:

http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/ucm109596.htm

4.3.3 Information about ACCO Folders:

Note: The vendor information found below is provided as an example of where these items may be purchased and is not intended as an endorsement of the vendor or a mandatory vendor to be used.

a. Example Vendor

1. Office Depot:

http://www.officedepot.com/a/products/193664/Acco-Presstex-60percent-Recycled-Binder-Side/

http://www.officedepot.com/a/products/193623/Acco-Presstex-60percent-Recycled-Binder-Side/

http://www.officedepot.com/a/products/102905/Acco-Presstex-60percent-Recycled-Binder-Side/
4.3.4 FDA Mailing Addresses

CDER
Central Document Room
Center for Drug Evaluation and Research
Food and Drug Administration
5901-B Ammendale Rd.
Beltville, MD 20705-1266

CBER
Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center,
HFM-99, Suite 200N
1401 Rockville Pike
Rockville, MD 20852-1448

4.4 Website Address Hyperlinks

All hyperlinks to websites included are operational as of the date of this document. Please contact the ICTR Research Navigator via the contact information below if any non-functional hyperlinks are identified so that they may be updated.

4.5 Questions and Additional Contact Information

For questions regarding any of the information presented or use of the template, please contact the ICTR Research Navigator at ICTR_Navigators@jhmi.edu or via telephone at 410-614-5383.
5.0 IND Withdrawal Submission

Cover Letter

[INSTRUCTIONS: The suggested format for the cover letter to accompany the request for IND withdrawal may be found below.]
Dear Reviewers,

Pursuant to 21 CFR 312.38, I am submitting a request to withdraw IND number [INSERT: IND number].

This withdrawal is requested because [INSERT: include short summary of why withdrawal is being requested (e.g. all clinical trials conducted under this IND have concluded, safety concerns, etc. NOTE: If the IND is being withdrawn because safety concerns, provide brief summary of the issues and state that all participating investigators and reviewing Institutional Review Boards have been notified of those specific issues.)] All participating investigators and their Institutional Review Boards have been notified of the IND withdrawal. All unused stock of the investigational agent, [INSERT: name of investigational agent], has been returned and disposed of appropriately.

If you have any questions about the material included in this submission, please do not hesitate to contact me at [INSERT: phone number of Sponsor-Investigator] or by email at [INSERT: email address of Sponsor-Investigator].

Sincerely,

[INSERT: Sponsor-Investigator Name]
[INSERT: Title]
[INSERT: Affiliation]

Enclosure:
[COMMENTS: A suggested format for the title page is provided below.]
Withdrawal of IND

DATE

IND Application Title:

Drug Product:

Serial Number:

Sponsor-Investigator:
Form FDA 1571

[SECTION INTRODUCTION: The requirements for this section of the submission are provided below. NOTE: Some information included may not be applicable in all cases. Suggested text, as well as web addresses for forms and guidance documents, is provided here.]
1.0 Form FDA 1571

[INSERT TEXT: “Please see the signed and dated Form FDA 1571 next.”]

[WEB ADDRESS TO FDA FORM AND FORM INSTRUCTIONS]

- **FDA form 1571:**
  

- **Instructions for form 1571:**
  

[Special Note: For this submission, check “Other (Specify)” in Box 11 insert “Withdrawal of IND” or “Withdrawal of IND for safety reasons” in the space provided. In Box 13, check boxes 1, 2, and 10.]
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Withdrawal of IND

[Regulatory Reference]  PART 312 -- INVESTIGATIONAL NEW DRUG APPLICATION

Subpart B--Investigational New Drug Application (IND)

Sec. 312.38 Withdrawal of an IND.

(a) At any time a sponsor may withdraw an effective IND without prejudice.

(b) If an IND is withdrawn, FDA shall be so notified, all clinical investigations conducted under the IND shall be ended, all current investigators notified, and all stocks of the drug returned to the sponsor or otherwise disposed of at the request of the sponsor in accordance with 312.59.

(c) If an IND is withdrawn because of a safety reason, the sponsor shall promptly so inform FDA, all participating investigators, and all reviewing Institutional Review Boards, together with the reasons for such withdrawal.]
3.0 Withdrawal of IND

[INSTRUCTIONS: A brief summary of the reason for withdrawing the IND should be provided here. If the IND is being withdrawn for safety reasons, please summarize those issues here. Include statement here to the effect that IND safety reports were previously submitted to FDA.]

3.1 Completion or closure of clinical trials under the IND

[INSTRUCTIONS: Provide here a list of the clinical trials performed under the IND and their dates of completion or closure.]

3.2 Notification of participating investigators and IRBs

[INSTRUCTIONS: Provide here a list of the participating investigators and sites notified of the IND withdrawal. (If the IND is being withdrawn for safety reasons, specifically state here that the participating investigators and their IRBs were notified of these issues). Reference an attachment (Section 4.0) which includes the IRB acknowledgement and study termination letters from each site including the site of the sponsor-investigator.]

3.3 Recall and disposal of unused stores of investigational agent

[Regulatory Reference
Sec. 312.59 Disposition of unused supply of investigational drug.]

The sponsor shall assure the return of all unused supplies of the investigational drug from each individual investigator whose participation in the investigation is discontinued or terminated. The sponsor may authorize alternative disposition of unused supplies of the investigational drug provided this alternative disposition does not expose humans to risks from the drug. The sponsor shall maintain written records of any disposition of the drug in accordance with 312.57.]

[INSTRUCTIONS: Provide a brief description here of the disposition of all unused stock of investigational agent. If not applicable, state same here.]
Attachments

4.0 Attachments

[INSTRUCTIONS: Include here IRB acknowledgements/study termination letters from participating sites and any other documentation/information pertinent to the sponsor-investigator’s decision to withdraw the IND that the FDA reviewers will need.]