Document Number: SOP-4-v5	Title: Administrative Letters
Effective Date: June 26, 2020	

1. DEFINITIONS

Term	Definition
Investigational New Drug Application (IND)	An IND application is submitted to FDA if a drug (or biological product) not previously authorized for marketing in the US is intended to be used for the purposes of clinical investigation or, in certain cases, for the purposes of clinical treatment when no approved therapies are available.
Medical Monitor	The investigator listed on Form FDA 1571 as the "person responsible for monitoring the conduct and progress of the clinical investigations"
Study Team	For the purposes of this SOP the study team is defined as including, but not limited to, the following individuals: PI, Clinical Development Associate, Regulatory Associate, IND Specialist (if applicable), Biostatistician, GMP Director (if applicable), Study Coordinator, Clinical Coordinator, Clinical Research Associate, Data Technician, Data Quality Coordinator, Regulatory Assistant, Co-Investigator, UNC Cancer Network Project Manager

2. BACKGROUND

During the course of a study, a protocol may require clarification based on misconceptions and/or misinterpretations of its written intent. According to the International Conference on Harmonization (ICH) Guidelines for Good Clinical Practice (GCP), "the investigator should not implement any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documentation approval/favorable opinion from the IRB/IEC of an amendment, except where necessary to eliminate an immediate hazard(s) to trial subjects, or when the change(s) involves only logistical or administrative aspects of the trial (e.g., change in monitor(s), change of telephone number(s))."

At Lineberger Comprehensive Cancer Center (LCCC), these types of administrative changes may be implemented via issuance of an Administrative Letter.

3. PURPOSE

This SOP describes when and how to initiate, draft, and implement Administrative Letters for LCCC investigator-initiated trials (IITs).

4. SCOPE

This SOP applies to all Investigator Initiated Trials (IITs) (UNC only or multicenter) that involve treatment with a pharmaceutical agent(s), are sponsored by LCCC, and are managed by the CPO, whether conducted under an IND or not.

Document Number: SOP-4-v5	Title: Administrative Letters
Effective Date: June 26, 2020	

5. RESPONSIBLE PARTIES

This SOP applies to individuals within the Clinical Protocol Office (CPO) involved in coordinating and managing LCCC IITs and individuals acting on behalf of the LCCC as a sponsor for the management of data, personnel, quality control, and regulatory affairs for LCCC IITs.

6. PROCEDURES

6.1. Request for a clarification of the protocol

Any member of the study steam at UNC or an affiliate site or the study drug manufacturer(s) (if applicable) directs a request to clarify the protocol to the Principal Investigator (PI).

6.2. Screening of the protocol clarification request by the PI and/or IND PI (if applicable) to determine if there is a critical need for the clarification and if an administrative letter is appropriate

The PI and/or Medical Monitor (if applicable) determine if there is a need for a clarification of the protocol at this time. With PI and/or Medical Monitor approval, requests to address non-critical clarifications, typographical errors, etc. may be pooled and held until such a time when a critical amendment is needed. An Administrative Letter may be written, as opposed to a full protocol amendment, for clarifications that do not change the original meaning of the protocol or for logistical/administrative changes. If a protocol amendment is required, please refer to SOP-2 Amending CPO IIT for guidance on protocol amendments.

6.3. Notification

Once the PI determines that the protocol will be amended per the request, the IND Specialist (if applicable) is notified of the upcoming administrative letter. The modification request is additionally tracked within OnCore.

6.4. Administrative letter drafted

The administrative letter is drafted by a member(s) of the study team.

6.5. Review of the administrative letter

Applicable members of the study team will review the administrative letter for accuracy and completeness. The clinical development team and clinical development management (if required or appropriate) review the administrative letter for appropriateness. If the change included in the administrative letter is limited to global institutional policy changes that require clarification relative to protocol operations or the addition and/or removal of co-investigators or medical monitor, then review and approval is not warranted. The feedback is incorporated into the administrative letter.

Document Number: SOP-4-v5	Title: Administrative Letters
Effective Date: June 26, 2020	

6.6. Approval of the administrative letter

The administrative letter is approved by the PI and/or Medical Monitor (if applicable). If required by the study contract, the administrative letter is distributed to the funding source for review and approval. Any required changes are incorporated into the administrative letter.

6.7. Finalization of the Administrative Letter

The administrative letter is finalized, signed and a pdf made of the letter.

6.8. Informed Consent Forms (ICF) updated (if applicable)

The ICFs are updated to reflect any clarifications in the administrative letter and are distributed to the PI and applicable team members for review and quality assurance. The study team reviews the ICF for complete and accurate updates.

6.9. Document Release

The finalized study documents are released to the study team.

6.10. Administrative Letter Distributed to all Sites

The administrative letter is also distributed to the multicenter sites (if applicable).

6.11. Institutional Review Board (IRB) Review and Approval

The administrative letter is submitted to all IRBs of record and the IRB's approval of the administrative letter, once received, is communicated to the study team.

6.12. Regulatory Submission Tracking of the Approved Administrative Letter

The IRB submission is documented in OnCore. Applicable cross-functional team members are notified of the approval of the administrative letter and of its contents. The administrative letter is attached in OnCore so that all cross-functional team members can easily access it.

The review and approval of their local IRBs is tracked.

6.13. Administrative letter content integrated into the protocol at the time of the next protocol amendment

If deemed appropriate by the PI in consultation with the clinical development team, the clarification within the administrative letter will be incorporated into the next protocol amendment.

Document Number: SOP-4-v5	Title: Administrative Letters
Effective Date: June 26, 2020	

7. RELATED DOCUMENTS AND FORMS

7.1. DT-4 Administrative Letter Template

8. REFERENCES

8.1. 21CFR312.30 IND Protocol Amendments

9. RESOURCES

9.1. Code of Federal Regulations IND Protocol Amendments (21CFR312.30): http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.30

9.2. IND Application Reporting: Protocol Amendments: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm362503.htm

9.3. International Conference on Harmonization (ICH) Guideline for GCP E6 (R1): https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf

10. APPROVALS

Medical Director

Carrie Lee — 7/31/2020 Date

11. Revision History

Revision No.	Date	Author	Reason for Change
1 (immaterial)	04/22/2014	L Zimmer	Added information on central storage and periodic review of Administrative Letters; other minor editorial changes
2 (immaterial)	06/04/2017	Kaitlin Morrison	Revised format to new SOP format guidelines; removed necessity to email administrative letter to the study team since it will be attached in Oncore; Removed required confirmation of receipt by UNC staff of emailed administrative letter because the letter will be attached in OnCore; changed references to NCTraSC IND Specialist to LCCC IND Specialist; removed annual quality assurance review of Administrative Letters by the Director of Regulatory Affairs because Quality Assurance will occur at the time that the letter is written

Document Number: SOP-4-v5	Title: Administrative Letters
Effective Date: June 26, 2020	

3	3/15/19	Kaitlin Morrison	Adjusted the timing of multicenter distribution to be consistent with current multicenter practice.
4 (immaterial)	06/25/2020	Kaitlin Morrison	Administrative changes to match language in the newly updated protocol amendment SOP