Vancouver CoastalHealth Research Institute

Standard Operating Procedure
Management of Investigational Products

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Site Approval

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Authorization to Adopt

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Document History

Version	Summary of Changes Made	Effective Date
1	Original document	09-JUL-2010
2	This version has undergone extensive revision for administrative, educational, regulatory, and clinical changes by individual content experts and the VCHRI SOP Committee. This document has also had substantial formatting, grammatical and glossary updates. It has been classed as a rewritten document.	10-JAN-2016
3	This version has undergone revision for administrative, education, regulatory and clinical changes by individual content experts and VCHRI SOP Committee. There have been changes made to 2.2, 6.1, 6.2.3, 6.3.4, 6.4, 6.9. References have been updated.	01-Jun-2021

1. PURPOSE

1.1. This Standard Operating Procedure (SOP) describes the management of Investigational Product(s) regardless of the source (e.g., includes commercially available products). This SOP describes receipt, labeling, storage, distribution, accountability, and return or authorized destruction of Investigational Product(s) which include drugs, biological products, natural health products, radiopharmaceuticals, and medical devices.

2. SCOPE

2.1. This SOP is applicable to those Research Team Members responsible for managing Investigational Product(s) for a Clinical Trial/Study conducted at the Institution.

2.2. The study Protocol should outline specific procedures for handling the Investigational Product(s). The term Investigational Product, as used in this SOP, includes drugs, biological products, natural health products, radiopharmaceuticals, and medical devices, as necessary.

3. RESPONSIBILITIES

3.1. The Principal Investigator or Sponsor-Investigator is responsible for ensuring that Investigational Product(s) are managed according to all of the applicable regulatory requirements, International Conference on Harmonisation (ICH) Good Clinical Practice (GCP), Good Manufacturing Practice (GMP), Sponsor, and local requirements.

3.2. Any or all parts of this procedure may be delegated to appropriately trained research team members, but remain the ultimate responsibility of the Principal Investigator or Sponsor-Investigator.

4. RELATED SOPS/DOCUMENTS

4.1. VCHRI Tool - Drug Accountability Log
4.2. VCHRI Tool - Drug Dispensing Log

5. DEFINITIONS

5.1. See VCHRI Glossary of Terms.

6. PROCEDURE

6.1. General

6.1.1. The Principal Investigator must sign and return the Research Agreement(s) and Health Canada's Qualified Investigator Undertaking form to the Sponsor, prior to the Sponsor's shipment of the Investigational Product to the Study Site. In addition, the Sponsor must update the Clinical Trial Site Information Form (CTA-A), if applicable, and file with Health Canada prior to the commencement of the Clinical Trial/Study.

6.1.2. If there are complex steps in the Investigational Product(s) management process (from receipt to dosing), develop a Working Practice document or study-specific SOP for the handling, preparation and/or transport of the Investigational Product(s).

6.2. Receipt and Inventory of Investigational Product(s)

6.2.1. Upon receipt of the Investigational Product(s), review the shipping documentation. Conduct an inventory the Investigational Product(s) received in order to ensure that the information on the shipment invoice corresponds to the Investigational Product(s) sent and received, including the quantity, lot number and expiry information, as applicable. Check the condition, and record any damage, problems and/or discrepancies. Document the inventory results and retain with the Essential Documents.

6.2.2. Communicate any inconsistency to the Sponsor or Sponsor-Investigator as soon as possible. Document and retain with the Essential Documents.

6.2.3. Retain all documentation related to transportation and receipt of the Investigational Product with the Essential Documents) throughout the Clinical Trial/Study.

6.3. Labeling and Coding of Investigational Product(s)

6.3.1. The manufacturing, labeling, packaging and shipping of Investigational Product(s) (including active comparator(s), placebos, and devices, as applicable) is the responsibility of the Sponsor or Sponsor-Investigator. In some instances, labeling responsibility may be delegated to a Clinical Trial/Study site-level Research Team Member.

6.3.2. Ensure that the label on Investigational Product(s) is not hidden/covered, withdrawn, or modified without the authorization of the Sponsor or Sponsor-Investigator.

6.3.3. Apply an additional label, if required by the Protocol or Institution (e.g., Participant name, Institution name, additional dosing instructions, or instructions on storage etc.). Do not cover the original label of the Investigational Product.

6.3.4. In order to respect Participant confidentiality, ensure there is no Participant-identifying information (nominative data) on the container or device labels, when/if medication is returned to the Sponsor or Sponsor-Investigator.

6.4. Storage of Investigational Product(s)

6.4.1. Store Investigational Product(s) in a secure environment (e.g. locked room) with controlled access restricted to authorized personnel. Refer to special storage conditions for biologics, radiopharmaceuticals, or devices, as needed. The Clinical Trial/Study site should have a documented procedure on how to correct environmental changes and have a storage and transfer contingency plan and procedure (e.g. plan and who should be notified, with their contact information).

6.4.2. Ensure that the storage location has appropriate and controlled temperature/humidity, as stated in the Protocol or other written information provided by the Sponsor or Sponsor-Investigator.

6.4.3. Monitor the temperature/humidity conditions, and record regularly, either manually or by an automatic device. Be prepared to move the Investigational Product(s) to an alternate storage area, if problems arise. Document any storage issues.

6.4.4. Keep storage records within easy access of the Investigational Product(s) and have it available for monitors, auditors, etc., if requested

6.4.5. File temperature records with Essential Documents study documentation at the end of the Clinical Trial/Study.

6.4.6. Check that temperature monitoring devices are valid (not expired) and calibrated throughout the Clinical Trial/Study. This should be noted in the equipment log.

6.5 Quarantine of Investigational Product(s)

6.5. Place any expired or any compromised (e.g. damaged, unmonitored or potentially compromised) Investigational Product(s) in a labelled container within a clearly labelled “Quarantine” section.

6.5.1. Maintain specified storage and environmental conditions specified in the Investigator Brochure and/or Protocol.

6.5.2. Follow the Sponsor’s instructions for usage, relabeling, return or destruction of Investigational Product(s) as applicable.

6.5.3. Document actions and maintain records and communications regarding the quarantine of the Investigational Product(s); file these records in the Site Master File or Investigational Product(s) folder.

6.5.4. Provide Sponsor or Sponsor-Investigator with written correspondence and records related to the quarantined IP.

6.6 Distribution/Dispensing the Investigational Product(s)

6.6.1. Use the Investigational Product(s) only in accordance with the approved Protocol. Document any use of the Investigational Product(s) not in accordance with the approved Protocol. Report to Sponsor or Sponsor-Investigator, as required.

6.6.2. Maintain a dispensing log to document assignment of Investigational Product(s) to specific study Participants.

6.6.3. Inform each Participant about the correct use of the Investigational Product(s). Inform the Participant of his/her responsibility to return all unused Investigational Product(s) (if applicable) and Investigational Product(s) packaging (bottle, container, syringe, etc.), even if empty, as specified in the Protocol. Document this interaction in the Source Documents.

6.6.4. Assess Participant compliance with the instructions at appropriate intervals, as per the Protocol.

6.7. Accountability for Investigational Product(s)

6.7.1. Document the return of all Investigational Product(s) and/or containers by Participants.

6.7.2. In the event of accounting inconsistency, perform a Participant or pharmacy follow-up, for the safety of the Participant. Document this inconsistency.

6.7.3. Maintain documentation of all Investigational Product(s) and/or empty containers returned by Participants; include this documentation with the Essential Documents.

6.7.4. The Investigational Product(s), once assigned, are never to be (re)assigned to another Participant within the Site, to a Participant outside the Clinical Trial/Study, or to a Participant at another site.

6.8. Return/Destruction of Investigational Product(s)

6.8.1. Return to the Sponsor, Sponsor-Investigator or distributor, any Investigational Product(s) that remain after Clinical Trial/Study completion or for product recall reasons. Follow the instructions in the Protocol or other study documents, as required.

6.8.2. Obtain written authorization from the Sponsor or Sponsor-Investigator for destruction of Investigational Product(s) at the Study Site, if applicable.

6.8.3. Ensure that the Institution or pharmacy has appropriate procedures for the destruction of Investigational Product(s), and that the destruction is performed in accordance with those procedures. Obtain a certificate or documentation of destruction, if required.

6.8.4. Return or destroy defective or outdated products in the same manner, unless otherwise requested by the Sponsor or Sponsor-Investigator.

6.8.5. File the return and/or destruction documentation with Essential Documents.

6.9. Randomization Procedure

6.9.1. Follow the randomization procedures as described in the Protocol.

6.9.2. During the Clinical Trial/Study, retain documents related to randomization in a sealed envelope that is easily identifiable, and in locked storage, separate from other study documents.

6.9.3. Retain all documents relating to randomization by external sources (e.g. Interactive Voice Response System (IVRS).

6.9.4. Ensure that the randomization code is broken only in accordance with the Protocol.

6.9.5. File randomization documentation with Essential Documents upon completion of the Clinical Trial/Study.

6.10. Blinded Trials Only: Unblinding Procedure

6.10.1. Confirm that the coding system for the Investigational Product(s) includes a mechanism that permits rapid identification of the Investigational Product(s) in case of a medical emergency, but does not permit detectable breaks of the blinding.

6.10.2. Follow the Protocol-specific instructions for unblinding the Investigational Product(s).

6.10.3. Promptly document and explain to the Sponsor or Sponsor-Investigator any premature unblinding such as accidental unblinding or unblinding due to a Serious Adverse Event/Drug Reaction. Inform Research Ethics Board as per their procedures.

6.10.4. File unblinding documentation with the Essential Documents

7. REFERENCE(S)

BC Freedom of Information and Protection of Privacy Act, [RSBC 1996, c. 165], as amended from time to time.

Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans,* TCPS-2 (2014), December 2014.

Department of Justice (Canada), Personal Information and Protection and Electronic Documents Act (PIPEDA), last emended November 1, 2018, current to February 13, 2019.

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Government of Canada, Food and Drug Regulations (C.R.C., c. 870). Part C, Division 2, Good Manufacturing Practices. Last amended June 17, 2019.

Government of Canada, Medical Device Regulations, SOR/98-282, May 7, 1998; last amended February 13, 2017, current to March 20, 2017.

Government of Canada, Natural Health Products Regulations, Part 4 Clinical Trials Involving Human Subjects, SOR/2003-196, June 5, 2003; last amended June 1, 2008, current to March 20, 2017.

Health Canada, Food and Drug Act, Part C, Division 5, Drugs for Clinical Trials Involving Human Subjects, (Schedule 1024), June 20, 2001.

Health Canada, Good Manufacturing Practices Guide for Drug Products (GUI-0001). February 28, 2018.

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Health Canada, Health Products and Food Branch Inspectorate, Guidance Document - Annex 13 to the Current Edition of the Good Manufacturing Practices Guidelines: Drugs Used in Clinical Trials (GUI-0036). December 1, 2009.

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), ICH Harmonised Guideline, Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice, E6 (R2), November 9, 2016.

Network of Networks (N2) Management of Investigational Products SOP010_09, Effective 15 May 2021.

Pharmaceutical Inspection Convention, Pharmaceutical Inspection Co-operation Scheme, Annexe 11, Computerised Systems.

US Food and Drug Administration, Code of Federal Regulations, Title 21, Volume 1:

- Part 11, Electronic Records; Electronic Signatures, (21CFR11).
- Part 50, Protection of Human Subjects, (21CFR50).
- Part 54, Financial Disclosure by Clinical Investigators, (21CFR54).
- Part 56, Institutional Review Boards, (21CFR56).
- Part 312, Investigational New Drug Application (21CFR312).
- Part 314, Applications for FDA Approval to Market a New Drug (21CFR314).

US Department of Health and Human Services, Code of Federal Regulations, Title 45, Part 46, Protection of Human Subjects (45CFR46).

US Department of Health and Human Services, Guidance for Industry: Computerized Systems Used in Clinical Investigations, May 2007.

8. ATTACHMENT(S)

None.