



WHO DOES THIS APPLY TO:

- Fabricators and packagers/labelers of investigational medicinal product.

KEY POINTS:

- This document provides guidance relevant to the fabrication and packaging/labeling of drugs for use in human clinical trial. It is based on the PIC/S Annex 13 and includes the changes necessary to meet Canadian requirements. Effective date: June 1, 2004.

Annex 2 to the Current Edition of the Good Manufacturing Practices Guidelines: Manufacture of Drugs Used in Clinical Trials is available online at:

http://www.hc-sc.gc.ca/dhp-mpps/compli-conform/clin-pract-prat/docs/cln_trials-essais_cln_tc-tm_e.html

• Required elements:

- A Quality System that is described in written procedures and available to the sponsor. Clear and adequate instructions and records should be maintained.
- Appropriate labeling, and systems to ensure blinding is achieved and maintained while allowing for the rapid identification of product names and batch numbers where necessary.
- Procedures for product release and retrieval, return and destruction of unused product.
- Tamper-evident packaging and appropriate shipping and storage. Inventory controls at the trial site.
- Changes to product specifications and manufacturing instructions during the development of a product must be fully controlled. Traceability of changes should be maintained.
- All personnel involved in the development of investigational medicinal products should be appropriately trained.
- Risks of cross-contamination must be minimized (as toxicity, potency and sensitizing potential of the product may not be fully understood). This impacts design of equipment and facilities, inspection/test methods, and acceptance limits to be used after cleaning.

• Definitions:

- Blinding: A procedure wherein one or more parties in the trial are kept unaware of the treatment assignment(s). Unblinding is the disclosure of the identity of blinded products.

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- Comparator product: Control or placebo used as reference in a clinical trial.
- Investigator: Person responsible to the sponsor for the conduct of the clinical trial at the clinical trial site.
- Sponsor: An individual, corporate body, institution or organization that conducts a clinical trial.

FAQs

1. Are manufacturers of investigational medicinal products required to follow all GMP Guidelines?

- Yes. Drugs intended for use in clinical trials in Canada are regulated under Division 5 of Part C of the *Food and Drug Regulations*. Section C.05.010 (j) requires the sponsor to ensure that drugs for use in clinical trials are manufactured, handled and stored in accordance with the applicable GMP requirements referred to in Divisions 2 to 4, except for sections C.02.019 (Finished Product Testing), and C.02.025 and C.02.026 (Samples). Sponsors of clinical trials shall ensure that imported drugs are fabricated and packaged/labeled in accordance with these requirements.

2. Are SOPs required for investigational medicinal product manufacturing?

- Yes. The Quality System should be described in written procedures available to the sponsor, taking into account the GMP principles and guidelines applicable to investigational medicinal products. For every manufacturing operation or supply there should be clear and adequate written instructions and written records.

3. What is an order?

- An order is a formally authorized written instruction to process, package and/or ship the required number of units of investigational medicinal product. This should be given by or on behalf of the sponsor to the manufacturer. The order must reference the Product Specification File and the relevant clinical trial protocol.

4. What is a Product Specification File?

- A Product Specification File is a reference file containing all the necessary files to draft the detailed written instructions on processing, packaging, quality control testing, batch release and shipping of an investigational medicinal product. The Product Specification File should be continually updated as development of the product advances.

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5. What are the labeling requirements for investigational medicinal product used in Canada?

- Annex 2 outlines detailed labeling requirements for investigational medicinal product in Canada. Requirements differ for general packages, product that has secondary packaging, and product in blister packs or small packaging units.

6. Is validation required for investigational medicinal product manufacturing?

- Production processes for investigational medicinal products are not expected to be validated to the extent necessary for routine production but premises and equipment are expected to be validated.

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