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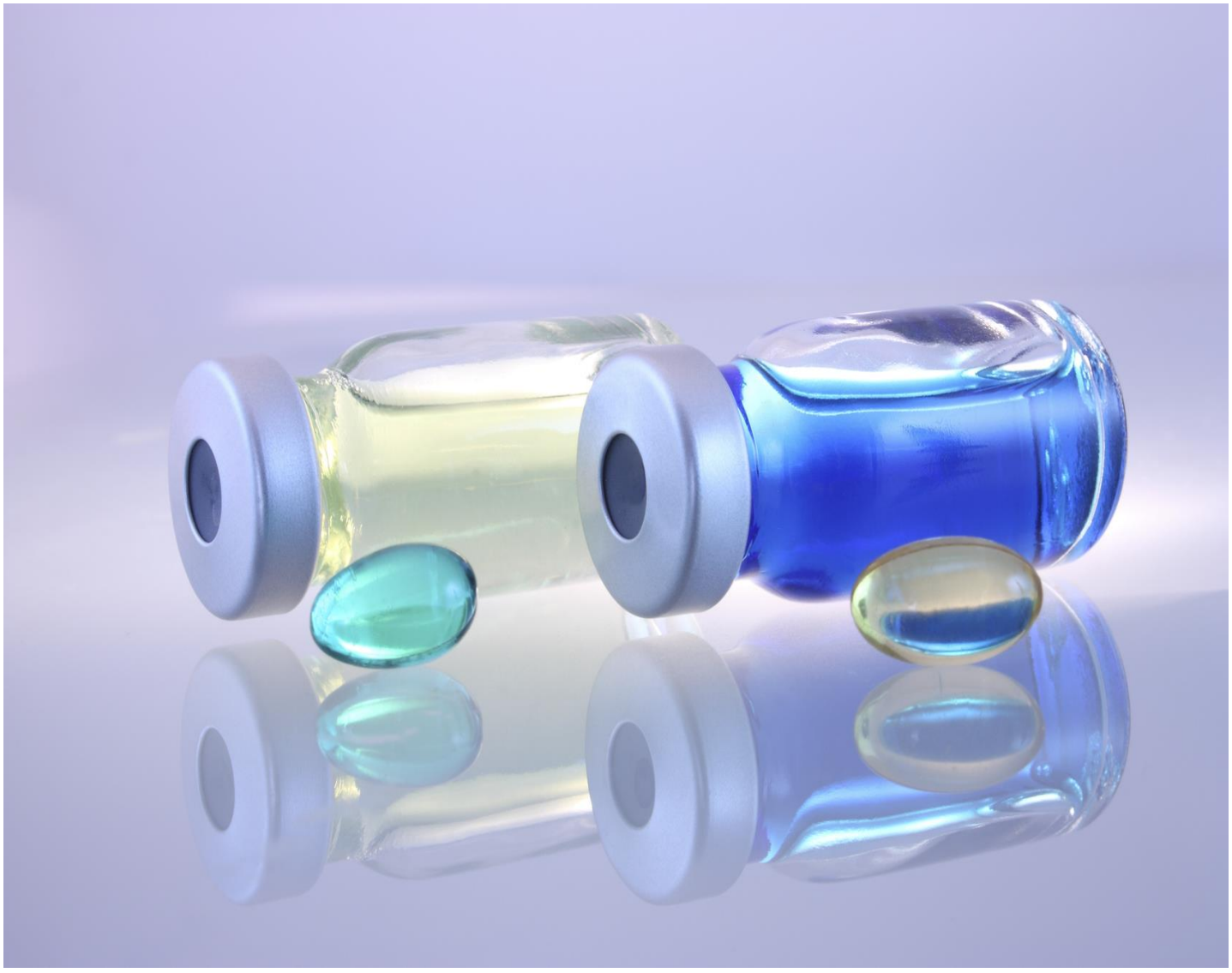
Annex 7 to the *Good manufacturing practices guide for drug products*- Selected non-prescription drugs



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Canada

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Également disponible en français sous le titre:
Annexe 7 du Guide sur les bonnes pratiques de fabrication – Lignes directrices sur certaines drogues en vente libre

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Disclaimer

This document does not constitute part of the *Food and Drugs Act* (the Act) or its regulations and in the event of any inconsistency or conflict between the Act or regulations and this document, the Act or the regulations take precedence. This document is an administrative document that is intended to facilitate compliance by the regulated party with the Act, the regulations and the applicable administrative policies.

Table of contents

The following table shows the types of icons used in this document, and the way they are intended to be used.

Important: Key or cautionary information for people to know.

Information: Supplementary information like quotes and legal references.

About this document

1. Purpose

This guide is for people who work with **selected non-prescription** drugs as:

- fabricators
- packagers
- labellers
- testers
- distributors
- importers

This document is an annex to the *Good manufacturing practices guide for drug products* (GUI-0001). You must read the two documents together to understand all relevant guidelines. These guides will help you understand and comply with Part C, Division 2 of the Food and Drug Regulations (the Regulations), which is about Good Manufacturing Practices (GMP). You can find definitions to terms used in this guide under Appendix A - Glossary.

Note: The previous version of this document focused solely on Category IV Monograph products. This document applies to an expanded list of drugs and, as such, the title has been changed to refer to “selected non-prescription drugs.”

2. Scope

This annex applies to the non-sterile, selected non-prescription drugs that are subject to Part C, Division 2 of the Food and Drug Regulations and have a Drug Identification Number (DIN):

- acne therapies (topical)
- antidandruff products
- antiseptic skin cleansers
- athletes foot treatment
- diaper rash products
- medicated skin care products
- mouthwashes
- sunscreen products
- throat lozenges

Many of the products listed above are considered as Category IV monographs, please see Non-prescription drugs: Category IV monographs. For each monograph, the following are specified: ingredients, strengths indications, directions for use, and warnings.

For imported products, the exemptions granted under the scope of a mutual recognition agreement (MRA) are limited to products that are considered drugs/medicinal products in their country of origin. If you are an importer, it is your responsibility to determine the classification of the product in the country of origin.

The scope of this document does not include products regulated by the Natural Health Products Regulations. For more information, please see the *Good Manufacturing Practices Guidance Document for natural health products*.

3. Introduction

The Food and Drug Regulations and *Good manufacturing practices guide for drug products (GUI-0001)* apply to all drugs. However, some interpretations in GUI-0001 may not apply in all situations such as with some personal care products. This annex to the current edition of GUI-0001 clarifies those aspects of GMP that are relevant to the fabrication, packaging/labelling, testing, importation and distribution of selected non-prescription drugs.

To avoid repetition, only those interpretations that are different from the ones in GUI-0001 are included in this annex. The numbering of each interpretation used in this annex corresponds to the numbering of the interpretation being modified from GUI-0001.

Unless otherwise stated in this annex, all interpretations included in the *Good manufacturing practices guide for drug products (GUI-0001)* also apply to selected Non-prescription drugs.

Guidance documents like this one are meant to help industry and health care professionals understand how to comply with regulations. They also provide guidance to Health Canada staff, ensuring that the rules are enforced in a fair, consistent and effective way across Canada.

Health Canada inspects establishments to assess their compliance with the *Food and Drugs Act* (the Act) and associated regulations. When we conduct an inspection, we will use this document as a guide in assessing your compliance with GMP requirements.

These guidelines are not the only way GMP regulations can be interpreted, and are not intended to cover every possible case. Other ways of complying with GMP regulations will be considered with proper scientific justification. Also, as new technologies emerge, different approaches may be called for.

Guidance documents are administrative and do not have the force of law. Because of this, they allow for flexibility in approach. So use this document to help you develop specific approaches that meet your unique needs.

Guidance

4. Modified interpretations

The following interpretations replace those in the *Good manufacturing practices guide for drug products (GUI-0001)*.

Personnel

C.02.006

Interpretation 1 in GUI-0001 associated with requirements for education and experience of personnel is replaced with the following to provide clarity in expectations for select non-prescription drugs.

1. The person in charge of your quality control department (if you are a fabricator, packager/labeller, tester, importer or distributor) and the person in charge of your manufacturing department (if you are a fabricator or packager/labeller):
    a. must hold:
        i. in the case of a fabricator, packager/labeller, or tester — a Canadian university degree or a degree recognized as equivalent by a Canadian university or Canadian accreditation body in a science related to the work being carried out
        ii. in the case of an importer or distributor — a diploma, certificate or other evidence of formal qualifications awarded on completion of a course of study from a university, college or technical institute in a science related to the work being carried out
    b. must have two years of practical experience in their area of responsibility
    d. may delegate duties and responsibility (for example, to cover all shifts) to a person who is qualified, while remaining accountable for those duties and responsibility:
        i. in the case of a fabricator, packager/labeller, or tester — the person must have a diploma, certificate or other evidence of formal qualifications awarded after completion of a course of study at a university, college or technical institute in a science related to the work being carried out, combined with at least two years of relevant practical experience.
        ii. in the case of an importer or distributor — the person must have necessary academic training and experience.

Sanitation

C.02.007

Interpretations 3.a and 3.e in GUI-0001 associated with cleaning validation requirements are replaced with the following:

3. a Clean primary contact surfaces for manufacturing and filling equipment in a way that consistently ensures there is no visible product or cleaning agent residues. Protect all equipment from contamination and keep it clean and dry. For throat lozenges, mouthwashes and other susceptible products, you should control the level of microbial contamination and ensure there are no objectionable micro-organisms.

3.e Ensure methods to detect residues or contaminants in evaluating cleaning are proven accurate and consistent. Demonstration of consistency should include a satisfactory analytical evaluation of parameters such as accuracy, precision and linearity for multiple tests of samples with known properties.

Raw material testing

C.02.009

Interpretation 3 in GUI-0001 associated with specifications of raw materials is replaced with the following:

3. Make sure your specifications of active pharmaceutical ingredients (APIs) comply with current versions of:

    a. the marketing authorization

    b. a recognized pharmacopoeia

        i. Where appropriate, include other properties or qualities not addressed by the pharmacopoeia (for example, particle size, polymorphs, density, etc.) in the specifications.

        ii. Where a recognized pharmacopoeia (Schedule B of the *Food and Drugs Act*) contains a specification for microbial content, include that requirement.

    House standard specifications for other raw materials are allowed if those standards comply with the drug's current marketing authorization.

Interpretation 4 in GUI-0001 associated with requirements for purified water is replaced with the following:

4. Ensure any water used in formulating a drug product for which there is a pharmacopoeial monograph (Schedule B of the *Food and Drugs Act*) meets the requirements of that pharmacopoeial monograph.

   When drugs do not appear in a pharmacopoeial monograph, the water used in their formulation must meet specifications based on sound physical and chemical principles. These specifications must include requirements for total microbial count, which should not exceed 100 colony-forming units (cfu)/ml. For oral preparations, ensure the absence of *Escherichia coli* and *Salmonella*. For topical preparations, ensure *Staphylococcus aureus* and *Pseudomonas aeruginosa* are absent.

Interpretation 7 in GUI-0001 associated with requirements to validate test methods is replaced with the following:

7. Ensure testing methods have been shown to provide accurate and consistent results. Demonstration of consistency should include a satisfactory analytical evaluation of parameters such as accuracy, precision and linearity for multiple tests of samples with known properties.

Interpretation 11 in GUI-0001 associated with requirements to test each container of a lot of raw material is replaced with the following:

11. In addition to the testing required in interpretation 9:
    a. Test each container of a lot of API for the identity of its contents using a specifically discriminating identity test.
    b. Instead of testing each container for identity, you may test a composite sample (derived from sampling each container), as long as you meet the following conditions:
        i. A suitable test exists.
        ii. The number of individual containers for each composite sample does not exceed 10.
        iii. A potency test is performed on each composite sample.
    c. Instead of testing each container for identity, you may test only a proportion of the containers, as long as there is evidence to ensure that no single container of API has been incorrectly labelled.
        i. Interpretation 11.c applies to API coming from a single product fabricator or plant. It also applies if it comes directly from a manufacturer (or in the manufacturer's sealed container) and there is a history of reliability. In this case, regular audits of the manufacturer's quality assurance system must be conducted by or on behalf of the purchaser/drug fabricator.
        ii. The available evidence should include an on-site audit report of the vendor by

a person who meets the requirements of interpretation 1 under section C.02.006 “Personnel.” The audit report should address at least the following:

- the nature and status of the manufacturer and the supplier, and their understanding of the GMP requirements of the pharmaceutical industry
- the quality assurance system of the raw material manufacturer
- the manufacturing conditions under which the raw material is produced and controlled

iii. Provided that you meet the requirements outlined in interpretations 11.b.i, you may conduct identity testing on representative samples. You should statistically determine the number of samples taken to prepare the representative sample and specify this number in a sampling plan. You should also define the number of individual samples that may be blended to form a composite sample, taking into account the nature of the material, knowledge of the supplier, and homogeneity of the composite sample.

iv. Interpretation 11.b does not apply when the API is supplied by intermediaries (such as brokers), where the source of manufacture is unknown or not audited.

d. Ensure each container in a batch is sampled and its contents positively identified when the raw material is handled in any substantial way (e.g. repackaged by a third party) after leaving the site of its fabrication.

Manufacturing control

C.02.011

Interpretation 13.b in GUI-0001 associated with validation of changeover procedures for fabrication or packaging/labelling of non-medicinal products is replaced with the following:

13. b. In some cases, similar non-medicinal products can be fabricated or packaged/labelled in areas or with equipment that is also used to produce pharmaceutical products. If this happens, changeover procedures must be effective, evaluated and approved before implementation.

Interpretations 22 to 24 in GUI-0001 associated with validation of critical production processes requirement is replaced with the following:

Process consistency

22. Ensure production processes produce consistent results. The person in charge of the quality control department must also approve these production processes. To

demonstrate consistency, include an evaluation of completed batch documents, in-process controls, finished product test results and additional testing for at least three consecutive batches (as appropriate).

23. Prepare, evaluate, approve and maintain a written report that includes the results and conclusions of the production processes' evaluation.

24. Before implementation, evaluate any changes to the production processes, equipment, materials, or suppliers that could affect product quality or process reproducibility.

C.02.012

Interpretation 12.b.i in GUI-0001 associated with validation responsibilities for analytical methods and production processes in written agreements is replaced with the following:

12. b. The agreement should include the following:

i. a description of who is responsible for:

- writing and approving raw materials, packaging materials and finished product specifications
- purchasing, sampling, testing and releasing raw materials and packaging materials
- writing and approving manufacturing and packaging master formulae
- undertaking production, quality and in-process controls
- ensuring testing methods have been shown to provide accurate and consistent results
- ensuring production processes produce consistent results
- overseeing the stability program
- overseeing transport and storage logistics and conditions
- preparing specific sections of the annual product quality review

Quality control department

C.02.015

Interpretation 8.e and 8.l.iv in GUI-0001 concerned with validation of test methods is replaced with the following:

8. e. All test methods have been shown to provide accurate and consistent results. A lab that is using a test method where the lab did not perform the original evaluation (e.g. the use of a compendial method) should verify the appropriateness of the test method. All

testing as described in the marketing authorization should be carried out according to the approved methods.

i. The transfer of test methodology from one lab to another should include an assessment to verify that the test method(s) complies with the marketing authorization. A gap analysis should be performed and documented to identify aspects to be verified before starting a technical transfer process.

ii. The transfer of test methodology should be described in a written protocol. This should include (but is not limited to) the following parameters:

- the relevant test method(s) undergoing transfer
- additional training requirements
- standards and samples to be tested by both labs
- any special processing, transport and storage conditions for test items
- the testing to be performed
- the acceptance criteria

iii. Deviations from the protocol should be investigated before closing the technical transfer process. The technical transfer report should document the comparative outcome of the process and should identify areas requiring further test method re-evaluation.

8.l.iv Technical aspects of the agreement must be drawn up by qualified personnel suitably knowledgeable in the relevant lab testing and GMP. The agreement must:

1. permit audit of the external lab's facilities and operations
2. clearly describe (at a minimum) who is responsible for:
    a. overseeing collection, transportation and storage conditions of samples before testing
    b. keeping stability samples at predetermined temperatures and humidity, if applicable
    c. testing methods to be used, limits and test method evaluation for accuracy and consistency
    d. retaining analytical results and supporting documentation (see additional guidance under C.02.021)

Finished product testing

C.02.018

Interpretation 2 in GUI-0001 associated with requirements to validate test methods is replaced with the following:

2. Ensure all test methods have been shown to provide accurate and consistent results according to the marketing authorization. Demonstration of consistency should include a satisfactory analytical evaluation of parameters such as accuracy, precision and linearity for multiple tests of samples with known properties.

C.02.019

In addition to Interpretation 4 in GUI-0001:

4. Buildings authorized by recognized countries or regions:
    a. If you are a distributor or importer of a drug included in column 1 of the list of Non-prescription Drugs for Which the Testing Requirements Set Out in Subsections C.02.019 (1) and (2) of the Food and Drug Regulations do not apply and that drug is fabricated, packaged/labelled in Canada or a recognized country or region and tested in a recognized country or region, the following applies:
        i. The fabricator, packager/labeller and tester must be identified and listed on your drug establishment licence (DEL). You can find additional guidance in Health Canada's guidance document, *How to demonstrate foreign building compliance with drug good manufacturing practices (GUI-0080).*
        ii. The drug in column 1 must only contain active ingredients set out in column 2 and each corresponding quantity must be set out in column 3 of the list of Non-prescription Drugs for Which the Testing Requirements Set Out in Subsections C.02.019 (1) and (2) of the Food and Drug Regulations do not apply.
        iii. The distributor or importer must retain a copy of the batch certificate for each lot or batch of the drug received to demonstrate that the drug complies with the finished product specifications. An example of an acceptable format is the *International Harmonized Requirements for Batch Certification* used with our MRA partners, but is also acceptable for the importation of these products.
        iv. Re-testing, including identity testing and confirmatory testing are not

required when the drug is fabricated, packaged/labelled and tested in a recognized country or region.

Note: If any licensable activity such as fabrication, packaging, labelling or testing is performed in a non-recognized country or region, the testing expectations once the product is received in Canada automatically revert to those described under the section for buildings in non-MRA countries.

b. If you are an importer of drugs listed in column 1 of the list of Non-prescription Drugs for Which the Testing Requirements Set Out in Subsections C.02.019 (1) and (2) of the Food and Drug Regulations do not apply which is from a recognized country or region you may ship the drugs directly to a person (i.e. retailer), other than an importer or distributor as long as the following requirements are met before importation:

    i. The importer must receive and review documentation to determine that the drug complies with the specifications and the master production document for that drug prior to the drug being made available for sale by the person the drug is shipped directly to.

    ii. The importer should have measures in place to ensure that all requirements of the Food and Drugs Regulations are met. This means identifying roles and responsibilities and having appropriate quality agreements between all parties including the foreign manufacturer, importer and person (i.e. the retailer), receiving the product (refer to section C.02.012 of this document for information on quality agreements).

Document review must allow the importer to be able to determine that the products meet their specifications. Examples include Certificate of Analysis (CoA), batch records and any other relevant documents.

C.02.020

Importers of drug products in the List of Non-prescription Drug for which the testing requirements set out in subsections C.02.019 (1) and (2) of the *Food and Drug Regulations* Do Not Apply must ensure that the drugs were manufactured in accordance with the Master Production Documents (MPD) prior to releasing for sale. Certificate of manufacture is considered an acceptable evidence (please refer to the *Good manufacturing practices guide for drug products (GUI-0001)* for additional information).

Stability

C.02.027

Interpretation 1 in GUI-0001 associated with requirements to make stability determinations in accordance to Health Canada and International Council on Harmonisation (ICH) guidelines is replaced with the following:

1. Determine the stability of a drug before any marketing takes place. Its stability should also be determined before making any significant changes to formulation, fabrication procedures or packaging materials that may affect the drug's shelf life. You should make this determination according to Health Canada and ICH guidelines.

Interpretation 9 in GUI-0001 associated with the requirement for validation of analytical test procedures in accordance with ICH guidelines is replaced with the following:

9. Ensure all test methods used for stability evaluation have been shown to provide accurate and consistent results. Demonstration of consistency should include a satisfactory analytical evaluation of parameters such as accuracy, precision and linearity for multiple tests of samples with known properties.

   Assays should be stability indicating (e.g. specific enough to detect and quantify degradation products and to distinguish between degraded and non-degraded materials). Ensure limits for individual specified, unspecified and total degradation products comply with the marketing authorization.

Interpretations 10 and 12 in GUI-0001, associated with the requirement for evaluation of stability data in accordance with ICH guidelines, is replaced with the following:

10. Ensure shelf life is assigned according to an appropriate statistical evaluation of stability data. Verify shelf life using additional long-term stability data, as these data become available.

12. For imported products, stability studies from foreign sites are acceptable if the data meet Health Canada guidelines for stability, and if the site can show GMP compliance. The importer/distributor's responsible quality function should ensure study protocols comply with the marketing authorization. They must also review, update and maintain the stability results.

C.02.028

Interpretation 3 in GUI-0001 associated with bracketing and matrixing in accordance with ICH for the continuing stability program is replaced with:

3. Enroll a minimum of one batch of every drug strength and container closure system into your continuing stability program each year the drug is produced. Consider packaging size in your choice of batches to be enrolled. You may apply the principle of bracketing and matrixing designs if justified.

Minor changes to the formulations (e.g. addition, deletion or substitution of a fragrance, flavour or colour) may be acceptable without new stability data. However, you must conduct ongoing stability studies on the revised formulation to show that the proposed change does not affect the quality of the drug product. You may conduct these studies while you market the modified product.

Appendix A – Glossary

Acronyms

API: Active pharmaceutical ingredient

cfu: colony forming units

CoA: Certificate of Analysis

DEL: Drug Establishment Licence

DIN: Drug Identification Number

DIN-HM: Homeopathic DIN

GMP: Good manufacturing practices

ICH: International Council for Harmonisation

MPD: Master Production Documents

MRA: Mutual Recognition Agreement

NOC: Notice of Compliance

NPN: Natural Product Number

WHO: World Health Organisation

Terms

These definitions explain how terms are used in this document. They supplement the definitions provided in the *Good manufacturing practices guide for drug products* (GUI-0001).

If there is a conflict with a definition in the *Food and Drugs Act* or the Food and Drug Regulations, the definition in the Act/Regulations prevails.

Active ingredient – A drug that, when used as a raw material in the fabrication of a drug in dosage form, provides its intended effect. (C.01A.001(1))

Active pharmaceutical ingredient - An active ingredient that is used in the fabrication of a pharmaceutical. (C.01A.001 (1))

Note: For the purpose of these guidelines, this definition also includes: an active ingredient that is used in the fabrication of a drug that is of non-biological origin and that is listed in Schedule C to the Act.

Batch (or lot) - A specific quantity of material produced in a process or series of processes so that it is expected to be homogeneous within specified limits. In the case of continuous production, a batch may correspond to a defined fraction of the production. The batch size can be defined either by a fixed quantity or by the amount produced in a fixed time interval. (ICH Q7)

Batch certificate – Means a certificate issued by the fabricator of a lot or batch of a drug that is either imported within the framework of a mutual recognition agreement or referred to on the List of Non-prescription Drugs Not Subject to Certain Testing Requirements, and in which the fabricator

(a) identifies the master production document for the drug and certifies that the lot or batch has been fabricated, packaged/labelled and tested in accordance with the procedures described in that document;

(b) provides a detailed description of the drug, including

(i) a statement of all properties and qualities of the drug, including the identity, potency and purity of the drug, and

(ii) a statement of tolerances for the properties and qualities of the drug;

(c) identifies the analytical methods used in testing the lot or batch and provides details of the analytical results obtained;

(d) sets out the addresses of the buildings at which the lot or batch was fabricated, packaged/labelled and tested; and

(e) certifies that the lot or batch was fabricated, packaged/labelled and tested

(i) in the case of a drug that is imported within the framework of a mutual recognition agreement, in accordance with the good manufacturing practices of the regulatory authority that has recognized those buildings as meeting its good manufacturing practices standards, or

(ii) in the case of a drug that is not imported within the framework of a mutual recognition agreement and that is referred to on the List of Non-prescription Drugs Not Subject to Certain Testing Requirements, in accordance with the requirements of Division 2. (C.01A.001(1))

An example of a batch certificate's content is also described in Health Canada's International Harmonized Requirements for Batch Certification which was developed with our MRA partners but is still relevant for products covered in Annex 7.

Batch number – (See lot number)

Bracketing - The design of a stability schedule such that only samples on the extremes of certain design factors (e.g. strength, package size) are tested at all-time points as in a full design. The design assumes that the stability of any intermediate levels is represented by the stability of the extremes tested. Where a range of strengths is to be tested, bracketing is applicable if the strengths are identical or very closely related in composition (e.g. for a tablet range made with different compression weights of a similar basic granulation, or a capsule range made by filling different plug fill weights of the same basic composition into different sized capsule shells). Bracketing can be applied to different container sizes or to different fills in the same container closure system. (ICH Q1A)

Certificate of analysis (CoA) - A document containing the name and address of the lab performing the test(s), name and specifications of the material(s), test(s) performed, test method(s) used, actual numerical results, approval date(s), signature of approver, and any other technical information deemed necessary for its proper use.

Certificate of manufacture – A document issued by a vendor to a distributor or importer that attests that a specific lot or batch of drug has been produced in accordance with its master production documents. Such certificates include a detailed summary of current batch documentation, with reference to respective dates of revision, manufacture, and packaging, and are signed and dated by the vendor's quality control department. For drugs that are fabricated, packaged/labelled and tested in MRA countries, the batch certificate is considered to be equivalent.

Change control – A written procedure that describes the action to be taken if a change is proposed *(a)* to facilities, materials, equipment, and/or processes used in the fabrication, packaging, and testing of drugs, or *(b)* that may affect the operation of the quality or support system.

Changeover procedure - A logical series of validated steps that ensure the proper cleaning of suites and equipment before the processing of a different product begins.

Critical process - A process that if not properly controlled may cause significant variation in the quality of the finished product.

Data - Means all original records and certified true copies of original records, including source data and metadata and all subsequent transformations and reports of this data, which are recorded at

the time of the activity and allow full and complete reconstruction and evaluation of the activity. (Adapted from WHO draft)

Distributor or manufacturer - A person, including an association or partnership, who under their own name, or under a trade, design or word mark, trade name or other name, word, or mark controlled by them, sells a food or drug. (A.01.010)

Divisions 1A and 2 to 4 apply to the following distributors:

a. a distributor of an active ingredient or a drug in dosage form that is listed in Schedule C to the Act; and

b. a distributor of a drug for which that distributor holds the drug identification number. (C.01A.003)

Dosage form – A drug product that has been processed to the point where it is now in a form in which it may be administered in individual doses, unless otherwise defined in the Food and Drug Regulations.

Drug - "drug" includes any substance or mixture of substances manufactured, sold or represented for use in:

a. the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state, or its symptoms, in human beings or animals,
b. restoring, correcting or modifying organic functions in human beings or animals, or
c. disinfection in premises in which food is manufactured, prepared or kept;

(Section 2 of the Food and Drugs Act)

In Division 1A and Division 2 of the Food and Drug Regulations, “drug” does not include a dilute drug premix; a medicated feed as defined in subsection 2(1) of the Feeds Regulations, 1983; an active ingredient that is for veterinary use and that is not an active pharmaceutical ingredient; an active pharmaceutical ingredient for veterinary use that is not required to be sold pursuant to a prescription and that is also a natural health product as defined in subsection 1(1) of the Natural Health Products Regulations; a drug that is used only for the purposes of an experimental study in accordance with a certificate issued under section C.08.015.. (C.01A.001 (2))

Drug establishment licence - A licence issued to a person in Canada to conduct licensable activities in a building which has been inspected and assessed as being in compliance with the requirements of Divisions 2 to 4 of the Food and Drug Regulations.

Drug identification number - A drug identification number (DIN) is an eight (8)-digit numerical code assigned by Health Canada to each drug product marketed under the Food and Drugs Act and Regulations. A DIN uniquely identifies the following product characteristics: manufacturer, brand

name, medicinal ingredient(s), strength of medicinal ingredients(s), pharmaceutical form, route of administration.

Fabricate – To prepare and preserve a drug for the purpose of sale. (C.01A.001(1))

Finished product – A product that has undergone all stages of production, including packaging in its final container and labelling.

Import – To import into Canada a drug for the purpose of sale. (C.01A.001(1))

Label – Includes any legend, word, or mark attached to, included in, belonging to, or accompanying any food, drug, cosmetic, device, or package (section 2 of the Act). As described in package/label, the action of labelling refers to affixing the inner or outer label to the drug. (C.01A.001)

List of Non-prescription Drugs Not Subject to Certain Testing Requirements – Means the document entitled List of Non-prescription Drugs for Which the Testing Requirements Set Out in Subsections C.02.019(1) and (2)of the Food and Drug Regulations Do Not Apply that is published by the Government of Canada on its website, as amended from time to time. (C.01A.001(1))

Lot – See Batch.

Lot number – Any combination of letters, figures, or both, by which any food or drug can be traced in manufacture and identified in distribution. (A.01.010)

Manufacturing batch record – Records demonstrating that the batch of a drug was fabricated in accordance with the approved master production documents.

Marketing authorization – A legal document issued by Health Canada, authorizing the sale of a drug or a device based on the health and safety requirements of the *Food and Drugs Act* and its associated Regulations. The marketing authorization may be in the form of a Notice of Compliance (NOC), Drug Identification Number (DIN), a device licence for classes II, III and IV medical devices, or a natural product number (NPN) or homeopathic DIN- HM (DIN-HM).

Master production documents (MPD) – Documents that include specifications for raw material, for packaging material and for packaged dosage form; master formula, sampling procedures, and critical processing related standard operating procedures (SOPs), whether or not these SOPs are specifically referenced in the master formula.

Matrixing – The design of a stability schedule such that a selected subset of the total number of possible samples for all factor combinations is tested at a specified time point. At a subsequent time point, another subset of samples for all factor combinations is tested. The design assumes that the stability of each subset of samples tested represents the stability of all samples at a given time point. The differences in the samples for the same drug product should be identified as, for example, covering different batches, different strengths, different sizes of the same container closure system, and possibly in some cases, different container closure systems. (ICH Q1A) The concept of matrixing may also apply in other areas such as validation.

MRA country – A country that is a participant to a mutual recognition agreement with Canada. (C.01A.001(1))

Mutual recognition agreement (MRA) – An international agreement that provides for the mutual recognition of compliance certification for Good Manufacturing Practices for drugs. (C.01A.001)

Original record – Data as the file or format in which it was originally generated, preserving the integrity (accuracy, completeness, content and meaning) of the record, e.g. original paper record of manual observation, or electronic raw data file from a computerised system. (MHRA GMP Data Integrity Definitions and Guidance for Industry March 2015)

Package – As described in 'package/label,' the action of packaging refers to putting a drug in its immediate container. (Adapted from C.01A.001(1))

Package/label – To put a drug in its immediate container or to affix the inner or outer label to the drug. (C.01.A.001(1)) This includes the repackaging and relabeling of previously packaged and labelled drugs.

Personal care products - a substance or mixture of substances which is generally recognized by the public for use in daily cleansing or grooming. Personal care products may fall into one of three regulatory categories in Canada: cosmetics, drugs or natural health products.

Person - Anyone other than an importer, e.g. Retailer.

Quarantine – The status of materials isolated physically or by other effective means pending a decision on their subsequent approval or rejection. (ICH Q7)

Recognized country or region means a country that is set out on the List of Foreign Countries and their Regulatory Authorities for the Application of Subsection C.02.019(5) of the Food and Drug Regulations that is published by the Government of Canada on its website, as amended from time to time.

Raw material – Any substance other than packaging material or an in-process drug that is intended for use in drug manufacture, including substances that appear in the master formula but not in the drug, such as solvents and processing aids.

Shelf life – The time interval during which a drug product is expected to remain within the approved specification provided that it is stored under the conditions defined on the label and in the proposed containers and closure.

Specifications – Means a detailed description of a drug, the raw material used in a drug, or the packaging material for a drug and includes:

(a) a statement of all properties and qualities of the drug, raw material or packaging material that are relevant to the manufacture, packaging, and use of the drug, including the identity, potency, and purity of the drug, raw material, or packaging material,

(b) a detailed description of the methods used for testing and examining the drug, raw material, or packaging material, and

(c) a statement of tolerances for the properties and qualities of the drug, raw material, or packaging material. (C.02.002)

Standard operating procedure (SOP) – A written procedure giving instructions for performing operations not necessarily specific to a given product or material but of a more general nature (e.g. equipment operation, maintenance and cleaning; validation; cleaning of premises and environmental control; sampling and inspection). Certain SOPs may be used to supplement product-specific master and batch production documents.

Test – To perform the tests, including any examinations, evaluations and assessments, as specified in the Division 2 of the Food and Drug Regulations.

Validation – A documented program that provides a high degree of assurance that a specific process, method, or system will consistently produce a result meeting pre-determined acceptance criteria. (ICH Q7)

Wholesaler – means a person who is not a distributor described in section C.01A.003 and who sells any of the following drugs other than at retail sale: (a) a drug in dosage form that is listed in Schedule C or D to the Act, a drug that is a prescription drug or a controlled drug as defined in section G.01.001; (b) an active ingredient; (c) a narcotic as defined in the Narcotic Control Regulations; or (d) a drug containing cannabis as defined in subsection 2(1) of the Cannabis Act. (C.01A.001 (1))

Appendix B – References

Laws and regulations

Food and Drugs Act
https://laws-lois.justice.gc.ca/eng/acts/f-27/

Food and Drug Regulations
http://laws-lois.justice.gc.ca/eng/regulations/C.R.C.%2C_c._870/

Natural Health Product Regulations
http://laws-lois.justice.gc.ca/eng/regulations/sor-2003-196/

Non-prescription drugs: Category IV monographs
https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/non-prescription-drugs-category-iv-monographs.html

Good Manufacturing Practices

Good manufacturing practices guide for drug products (GUI-0001)
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-manufacturing-practices/guidance-documents/gmp-guidelines-0001.html

Good manufacturing practices for active pharmaceutical ingredients (GUI-0104)
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/information-health-product/drugs/guidelines-active-pharmaceutical-ingredients-0104.html

International guidance documents

ICH Q1A-E: Stability Testing of New Drug Substances and Products
https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/international-conference-harmonisation/quality.html

International Harmonized Requirements for Batch Certification
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/international/mutual-recognition-agreements/international-harmonized-requirements-batch-certification.html

Mutual recognition agreements
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/international/mutual-recognition-agreements.html