

Good manufacturing practices guide for drug products

GUI-0001 Health Canada

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This summary was prepared by the Rx-360 Monitoring and Reporting Working Group which tracks regulatory, legislative and policy developments relevant to pharmaceutical/medical device supply chain integrity. The summary is not intended to serve as comprehensive and formal interpretation or guidance (and should not replace your own review and analysis of any referenced source documents). If you have questions, please contact Brittany Tobery, Rx-360 Secretariat, at 301-710-9399 or btobery@rx-360.org.

About this document

1. Purpose - Guide for people who work with drugs as:

- Fabricators
- Packagers
- Labelers
- Testers
- Distributors
- Importers
- Wholesalers

Out of Scope:

- Establishment licensing
- Active pharmaceutical Ingredients (APIs)

2. Scope-Guidelines apply to these types of drugs:

- Pharmaceutical
- Radiopharmaceutical
- Biological
- Veterinary

3. Introduction

- Interpret the requirements for good manufacturing practices (GMP) in Part C, Division 2 of the Regulations
- Developed by Health Canada in consultation with stakeholders
- Written to harmonize with:
 - World Health Organization
 - Pharmaceutical Inspection Cooperation/Scheme (PIC/S)
 - International Council on Harmonization (ICH)
 - International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (VICH)
 - Other regulatory agencies in other countries

Checklist-GMP regulations by activity

Checklist – GMP regulations by activity

Chart 1.0: GMP regulations applicable to which licensable activities

Section	Regulation	F	P/L	I	D	W	T
Premises	C.02.004	✓	✓	✓	✓	✓	
Equipment	C.02.005	✓	✓				✓
Personnel	C.02.006	✓	✓	✓	✓	✓	✓
Sanitation	C.02.007	✓	✓				
	C.02.008	✓	✓				
Raw material testing	C.02.009	✓					*
	C.02.010	✓					*
Manufacturing control	C.02.011	✓	✓	✓	✓		
	C.02.012	✓	✓	✓	✓	✓	
Quality control department	C.02.013	✓	✓	✓	✓	✓	
	C.02.014	✓	✓	✓	✓	✓	
	C.02.015	✓	✓	✓	✓	✓	✓
Packaging material testing	C.02.016	✓	✓				*
	C.02.017	✓	✓				*
Finished product testing	C.02.018	✓	✓	✓	✓		*
	C.02.019		✓	✓	✓		*
Records	C.02.020	✓	✓	✓	✓		✓
	C.02.021	✓	✓	✓	✓	✓	✓
	C.02.022			✓	✓	✓	
	C.02.023	✓	✓	✓	✓	✓	
	C.02.024	✓	✓	✓	✓	✓	
	C.02.025	✓		✓	✓		
Samples	C.02.026	✓		✓	✓		
	C.02.027			✓	✓		*
Stability	C.02.028			✓	✓		*
	C.02.029	✓	✓				*

* Where applicable, depending on the nature of the activities.

F = Fabricator

P/L = Packager/Labeller

I = Importer (MRA and non-MRA)

D = Distributor

W = Wholesaler

T = Tester

About quality management

4. Pharmaceutical quality system

- Guiding principles
- Developing a pharmaceutical quality system
- Good manufacturing practices for drugs
- Quality control
- Quality risk management

Guidance

5. Regulations

- **C.02.002**
 - Medical gas
 - Packaging material
 - Specifications
 - Properties and qualities
 - Detailed description of methods
 - Statement of tolerances for properties and qualities
- **C.02.002.1**
 - Antimicrobial agents

Guidance

5. Regulations

Sale

- **C.02.003**
 - Distributor
 - Importer
- **C.02.003.1**
 - Fabrication
 - Packaged/labelled
 - Tested
 - Stored
- **C.02.003.2**
 - Active ingredient import to Canada
 - Lot or batch label requirements in Canada

Guidance

5. Regulations

Use in fabrication

- **C.02.003.3**
 - Active ingredient use in fabrication

Premises

- **C.02.004**
 - Premises operations conditions
 - Surface cleaning
 - Prevention of contamination

Guidance

5. Regulations—*Premises*

- ***Rationale***
 - Establishment design/construction
- ***Interpretation***
 1. Design
 2. Pest/extraneous material
 3. Contamination prevention
 4. Temperature/humidity control
 5. Good sanitary practices
 6. Material flow
 7. Validation Master Plan
 8. Liquid/gases distribution systems
 9. Maintenance/repair
 10. Equipment/control system protection
 11. Product contamination minimization

Guidance

5. Regulations—*Equipment*

- **C.02.005**
 - Equipment design/ fabrication/ packaging/ labelling or testing
- ***Rationale***
 - Contamination prevention requirements
- ***Interpretation***
 1. Design, construction, location
 2. Extraneous material
 3. Contamination prevention
 4. Equipment repair
 5. Intended purpose

Guidance

5. Regulations—*Personnel*

- **C.02.006**
 - Personnel who supervise of every lot/batch
- ***Rationale***
 - Senior management responsibility
- ***Interpretation***
 1. Canadian quality control department requirements
 2. Wholesaler quality control requirements
 3. Packaging operations personnel requirements
 4. Secondary labelling and quality control requirements
 5. Personnel qualification requirements
 6. GMP personnel awareness
 7. Contractor/consultant qualifications

Guidance

5. Regulations—*Sanitation*

- **C.02.007**
 - Personnel who fabricate or package/label
- ***Rationale***
 - Written sanitation program assurance of cleanliness
- ***Interpretation***
 1. Written sanitation program
 2. Quality risk management principles
 3. Program effectiveness
 4. Personnel requirements
 5. Containment of dusty operations

Guidance

5. Regulations—*Sanitation*

- **C.02.008**
 - Health and hygienic minimum requirements
- ***Rationale***
 - Employee health, behavior and clothing contamination contribution
- ***Interpretation***
 1. Minimum health requirements
 2. Clothing requirements for staff and visitors

Guidance

5. Regulations—*Raw Materials Testing*

- **C.02.009**
 - Lot/batch of raw material testing
- ***Rationale***
 - Confirms identity, quality, quantity or yield
- ***Interpretation***
 1. Raw material covered by specifications
 2. Specification inclusions
 3. Specification compliance
 4. Purified water
 5. Water for injection
 6. Gas grade
 7. Test method validation
 8. Impurity specifications
 9. Representative test sampling
 10. Sampling procedures
 11. Raw material identity
 12. Raw material release
 13. Material vendors

Guidance

5. Regulations—*Raw Materials Testing*

- **C.02.010**
 - Testing
- ***Rationale***
 - Options for carrying out testing
- ***Interpretation***
 1. Testing other than identity testing
 2. Identity testing
 3. Raw material for confirmatory testing
 4. Transportation and storage conditions
 5. Different batches are separate for purposes of sampling, testing, and release
 6. Same batch received later on is considered a separate batch for sampling, testing and release

Guidance

5. Regulations—*Manufacturing control*

- **C.02.011**
 - Written procedures for drug specifications
- ***Rationale***
 - Product integrity maintenance
- ***Interpretation***
 - General
 - Validation
 - Validation master formula
 - Packaging master formula
 - Manufacturing operations
 - Packaging operations
 - Finished products
 - Annual product quality review

Guidance

5. Regulations—*Manufacturing control*

- **C.02.012**
 - Control systems
- ***Rationale***
 - Product recall
- ***Interpretation***
 - Recall
 - Self-inspection
 - Outsourced activities
 - The contract giver
 - The contract acceptor
 - Agreement

Guidance

5. Regulations—*Quality control dept.*

- **C.02.013**
 - Canadian quality control department requirements
- ***Rationale***
 - Quality unit independent of production fulfills both quality assurance and quality control responsibilities
- ***Interpretation***
 1. On site or accessibility to on-site quality control personnel
 2. Workspace, trained personnel, materials and equipment
 3. Approved written procedures
 4. Access to production areas

Guidance

5. Regulations—*Quality control dept.*

- **C.02.014**
 - Quality control department approval
- ***Rationale***
 - Quality control responsibility for approval of all raw materials, packaging materials and finished products
- ***Interpretation***
 1. Quality control department signatory
 2. Assessment for release of finished products
 3. Quarantine of raw materials/packaging materials
 4. Returned goods destruction
 5. Quarantine of rejected materials and products
 6. Lot/batch rework approval
 7. Reprocessing approval

Guidance

5. Regulations—*Quality control dept.*

- **C.02.015**
 - Quality control department examination of all fabrication, packaging/labelling, testing, storage, transportation and procedures that may affect drug quality
- ***Rationale***
 - Independent examination
- ***Interpretation***
 1. Person in charge of quality control
 2. Written agreements
 3. Storage and transportation guidelines
 4. SOPs and records for shipping/receiving
 5. Sampling
 6. Complaint assessment
 7. Change control system
 8. Lab test GMP requirement compliance

Guidance

5. Regulations—*Packaging material testing*

- **C.02.016**
 - Packaging material lot/batch testing
- ***Rationale***
 - Drug quality directly dependent upon packaging quality
- ***Interpretation***
 1. Each packaging material covered by specifications.
 2. Specifications compliance
 3. Primary/printed packaging material vendors
 4. Approved suppliers
 5. Released packaging use
 6. Obsolete packaging material segregation
 7. Sampling plan
 8. Sampling precautions

Guidance

5. Regulations—*Packaging material testing*

- **C.02.017**
 - Examination/testing sample
- ***Rationale***
 - Printed packaging and label examination
- ***Interpretation***
 1. Testing/examination after receipt on site
 2. Lot use prior to test completion
 3. Transportation/storage conditions
 4. Label/other printed material examination after receipt on site
 5. Positive identified of all primary packaging materials
 6. Each batch considered separate for testing purposes

Guidance

5. Regulations—*Finished product testing*

- **C.02.018**
 - Lot/batch drug testing against specifications
- ***Rationale***
 - Finished product tests complement controls used during manufacturing process
- ***Interpretation***
 1. Specification approval
 2. Test method validation
 3. Test performance
 4. Noncompliance quarantine

Guidance

5. Regulations—*Finished product testing*

- **C.02.019**
 - Packager/labeler, distributor, and importer requirements
- ***Rationale***
 - Testing options vary
- ***Interpretation***
 1. Packager/labeler identity confirmation
 2. Canadian buildings only
 3. MRA partners
 4. Testing non-MRA batches
 5. Positive identification requirements
 6. Process parametric release

Guidance

5. Regulations—*Finished product testing*

Chart 2.0: Periodic confirmatory testing for drugs from a non-MRA Country

	Buildings not subject to regulatory oversight by a PIC/S Participating Authority	Buildings subject to regulatory oversight by a PIC/S Participating Authority
Initial Testing Requirements	Test the first five unique lots of any drug received from each foreign building. ¹	N/A
Each drug	Carry out confirmatory testing in a manner that ensures at least one lot of each drug is tested in the first year it is received on the premise in Canada. ¹	N/A
Periodic Testing Requirements	Perform complete testing on at least one lot per year for each dosage form from each fabricator. Where multiple drugs are received from the same fabricator, carry out confirmatory testing for each drug at least once every five years.	

¹ For facilities qualified prior to the implementation of this guide you should take steps to ensure testing of five unique lots of any drug has been completed and that at least one lot of each drug has been tested.

Guidance

5. Regulations—*Records*

- **C.02.020**
 - Fabricator, packager/labeler, distributor, and importer record requirements
- **C.02.021**
 - Retention requirements
- **C.02.022**
 - Recall requirements
- **C.02.023**
 - Complaint record requirements
- **C.02.024**
 - Self-inspection record requirements

Guidance

5. Regulations—*Records*

- **C.02.024.1**
 - Fabricator, packager/labeler, wholesaler, and importer of active ingredient documentation requirements
- ***Rationale***
 - Documentation system must establish, control, monitor and record all activities
- ***Interpretation***
 1. Canadian language requirements
 2. FDA document requirements
 3. GMP SOPs
 4. Quality control approval
 5. Data integrity governance
 6. Electronic system requirements
 7. Electronic signature
 8. Document maintenance
 9. Sales record requirements
 10. Complaints/follow-up
 11. Specs/raw material test results
 12. Packaging specifications
 13. Personnel employed in GMP
 14. Record retention

Guidance

5. Regulations—*Samples*

- **C.02.025**
 - Sample retention

Guidance

5. Regulations—*Samples*

- **C.02.026**
 - Sample amount
- ***Rationale***
 - Samples for re-examination if product quality concerns arise
- ***Interpretation***
 1. Distributor--Samples for each lot/batch of finished product
 2. Drug fabricator—Samples for each lot/batch of raw material
 3. Sample retention management
 4. Sample quantity to allow duplicate testing
 5. Testing capacity
 6. Alternate sample retention (outside of Canada) consideration

Guidance

5. Regulations—*Stability*

- **C.02.027**
 - Period of time a packaged drug is in compliance with specifications
- ***Rationale***
 - Shelf life determination
- ***Interpretation***
 1. Stability timing
 2. Stability protocols
 3. Monitoring
 4. Bracketing/matrix rationale
 5. Limits of extended hold times
 6. Stability test parameters
 7. Antimicrobial preservative effectiveness
 8. Data availability
 9. Test validation
 10. Shelf life assignment
 11. Shelf life based on stability
 12. Foreign site study acceptability
 13. Reworked lot stability data

Guidance

5. Regulations—*Stability*

- **C.02.028**
 - Importer/fabricator monitoring
- ***Rationale***
 - Provides evidence that product will remain within specifications under recommended storage conditions
- ***Interpretation***
 1. Protocol available/implemented
 2. Scientific justification of differences
 3. Minimum requirements
 4. Long term studies
 5. Testing intervals
 6. Worst-case scenarios
 7. Out Of Specification
 8. Foreign sites
 9. Sterile products
 10. Multi-dose sterile products
 11. Stability evaluation
 12. Preservative

Guidance

5. Regulations—*Sterile products*

- **C.02.029**
 - Sterile requirements
- ***Rationale***
 - Minimize risk of microbiological, particulate and pyrogen contamination
- ***Interpretation***

Annex 1 to Good manufacturing practices guide—Manufacture of sterile drugs (GUI-0119)

Guidance

5. Regulations—*Medical gases*

- **C.02.030**
 - Provisions of C.02.025, c.02.027 and C.02.028 do not apply
 - Sections C.02.026 and C.02.029 do not apply
- ***Interpretation***

See Good manufacturing practices for medical gases (GUI-0031)

Appendices

- Appendix A—Glossary
- Appendix B—Questions and answers
- Appendix C--References

Thank you

For More Information



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