

Quick NOTES

Changes to HPFBI Good Manufacturing Practices (GMP) Guidelines (GUI-0001)

MARCH 2011
A Comparison between GMP
GUI-001 2009 and Version 2
(updated 3 May 2011)

WHO DOES THIS APPLY TO:

- For pharmaceutical, radiopharmaceutical, biological, veterinary and disinfectant drugs:
 - Fabricators
 - Packagers/labellers
 - Distributors
 - Importers
 - Wholesalers
 - Testers

KEY POINTS:

- Revised Good Manufacturing Practices (GMP) Guidelines 2009 Edition, Version 2 (GUI-0001) was posted March 4, 2011.
- Supersedes: 2009 Edition
- Date issued: March 4, 2011
- Date of implementation: March 4, 2011

SIGNIFICANT CHANGES IN VERSION 2:

- Wholesalers are now required to have a Quality Control Department.
- Additional details regarding handling, communication and documentation of complaints. Broadening of the definition of complaints to include 'any information respecting the quality of a drug or its deficiencies or hazards.' Quality Assurance agreements must now specify responsibilities for handling of complaints.
- Electronic systems for creating, modifying, or storing records must be validated.
- Additional detail regarding regular particulate and viable monitoring in Grade A and B areas.
- New interpretations pertaining to crimping requirements.

Good Manufacturing Practices (GMP) – 2009 Edition, Version 2 (GUI-0001)
is available online at:

<http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/docs/gui-0001-eng.php>



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SECTION-BY-SECTION REVIEW OF CHANGES

Regulation C.02.002

- Removed definition of Quality Control Department (now defined in Appendix B – Glossary of Terms).

Sale C.02.003

- No changes

Premises C.02.004

- Regulation (revised): “The premises in which a lot or batch of a drug is fabricated, packaged/ labelled **or stored...**” (**Bolded** content was added.)

Equipment C.02.005

- No changes

Personnel C.02.006

- No changes

Sanitation C.02.007, C.02.008

- C.02.007 Interpretation 2.2 (revised): Sanitation program must describe “requirements applicable to processing equipment” (no longer “cleaning requirements”).
- C.02.008 Interpretation 1.1 (revised): Where an employee is found to be a carrier of a communicable disease, the company must contact Health Canada and perform a risk assessment to determine if there is any product impact (a new requirement).

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Raw Material Testing C.02.009, C.02.010

- C.02.009 Interpretation 6.2 (revised): An additional condition has been added for reduced identity testing:
 - 6.2.1 (new): “a suitable test exists.”
- C.02.009 Interpretation 6.3 (revised): Reduced identity testing is now acceptable where **evidence is available** to ensure that no single container of raw material has been incorrectly labelled. (**Bolded** content replaces requirement for a validated procedure.)
 - 6.3.3 (revised): Available evidence (no longer validation) 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” to address the defined aspects per this section.

Manufacturing Control C.02.011, C.02.012

- No changes

Quality Control Department C.02.013, C.02.014, C.02.015

- C.02.013 Regulation (revised): Wholesalers must have on their premises in Canada a quality control department that is supervised by qualified personnel per C.02.006. The department does not have to be a distinct organizational unit.
- C.02.014 Regulation (revised): Wholesalers are still exempt from product release procedures.

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Quality Control Department C.02.013, C.02.014, C.02.015 (continued)

- C.02.015:
 - Regulation (revised): Content has been updated for clarification (previous version was incomplete), to broaden the definition of complaints, and to delineate responsibilities.
 - Regulation (2) (**bolded** content is revised): “The person in charge of the **quality** control department shall cause to be investigated any complaint **or information** that is received respecting **the quality of a drug or its deficiencies or hazards** and cause **any necessary** corrective action to be taken, **in the case where the complaint or information relates to an activity over which the department exercises quality control.**”
 - Regulation (2.1) (new): The quality control department that receives a complaint or related information forwards that complaint or information to the person in charge of the quality control department that exercises quality control over the related activity.
 - Interpretation 2 (new): Quality agreements must specify responsibilities related to the handling of complaints.

Packaging Material Testing C.02.016, C.02.017

- No changes

Finished Product Testing C.02.018, C.02.019

- No changes

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Records C.02.020 – C.02.024

- C.02.023:
 - Changes align this section with the requirements for addressing complaints per Section C.02.015.
 - Regulation (1) (revised): In the case of a complaint or information for an activity not under the control of the quality control department, the department records the name and business address of the person in charge of the quality department to whom the information was forwarded and the date on which it was forwarded.
- C.02.024:
 - Interpretation 1 (new): An electronic system used to create, modify or store records required to be maintained under these Regulations should be validated for its intended use.
 - Interpretation 4 (revised): Wholesalers are now included in the requirement to maintain records of complaints or any information respecting the quality of a drug or its deficiencies or hazards, and of subsequent investigations, including corrective actions taken.

Samples C.02.025, C.02.026

- C.02.025 interpretation 1.4 (revised): Retention samples may be stored at another Canadian site; the interpretation no longer specifies a site that holds a drug establishment licence.

Stability C.02.027, C.02.028

- C.02.028 interpretation 1 (revised): The list of parameters that should be included in a stability program has been expanded to include:
 - Reference to the manufacturing master formula and the packaging master formula.
 - Orientation of samples reflective of the worst-case scenario.

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Sterile Products C.02.029

- Personnel (interpretation 54): In Grade A and B areas, sterilized gowns that cover the skin and hair, plus sterilized protective goggles, are now required.
- Sanitation (interpretation 69.2): In Grade A and B areas, regular monitoring for particulates and viables should be performed during setup and all production operations (previously specified during each operating shift).
- Further detail was also added to interpretation 69.2: “Low values for contaminants are reliable only when a large number of air samples are taken. Adequate data is available to generate confidence that the required conditions are met throughout the duration of the operations. Where justified, cascade sampling strategies for active air and particulates (e.g., sampling continuously through a rotation of sampling sites) may be acceptable. Settle plates should always be present in the critical zone.”
- Aseptic Filling Operations (interpretation 80.11): New content regarding crimping requirements per PIC/S document, *Technical Interpretation of Revised Annex 1 to PIC/S GMP Guide*:
 - For aseptically filled vials, the filling/stoppering must be performed under Grade A conditions with a Grade B background.
 - If crimping does not take place in the aseptic core, stoppered vials should be protected with a Grade A air supply within a minimum of a Grade D environment until the cap has been crimped.
 - Crimping should be done as soon as possible after stoppering.
 - Distance between the exit of the Grade A/B to the actual point of crimping in the lower environment should be as short as possible.
 - Ensure procedures are in place to ensure that the stoppers are properly seated prior to crimping.
 - Document line stoppages and time lapses.
 - Segregate and dispose of stoppered vials that are not crimped within the established time lapse.

Medical Gases C.02.030

- No changes

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Appendices

- Appendix B – Glossary of Terms:
 - New definitions for:
 - Grade A Air Supply
 - Quality Control Department
 - Revised definitions for:
 - Dilute Drug Premix
 - Drug Establishment Licence
 - Drug Identification Number

FREQUENTLY ASKED QUESTIONS

1. Is there an implementation period for this update to the GMPs?

No. The updated guidelines are effective March 4, 2011, the day they were posted.

2. How do I meet the new requirements for wholesalers?

Wholesalers need to create/implement a Quality Control department that is:

- Supervised by a person qualified by pertinent academic training and experience.
- Responsible for the implementation and maintenance of a quality system as detailed in the GMPs.

The department's activities should include:

- Submitting/amending DEL applications.
- Hosting Health Canada inspections.
- Implementing/maintaining quality procedures and quality records.
- Addressing deviations, change controls, returned product.
- Collecting GMP evidence from suppliers.
- Ensuring your facility meets GMP requirements.

Quality & Compliance Services Inc. can help you with all of these activities.

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3. What's required to validate my electronic system?

Validation should include verification and/or a challenge of the following functions, as applicable to the specific electronic system:

- Data input and record creation.
- Viewing and output/reporting of data/records.
- Operations (proper sequence; second verification; data review and approval): handling of orders, procurement, purchases; notifications.
- Security (audit trails, electronic signatures, user levels, password aging and timeouts, card control).
- Data backup, changes to data, and change control.
- Database/system administrator operations (user maintenance and monitoring).

This requires computer validation protocols – Installation Qualification (IQ), Operational Qualification (OQ) and Performance Qualification (PQ) – and a validation final report

Q&C can perform these required validation activities for you.

4. What should I do differently for handling complaints?

- Ensure the quality control (QC) department is responsible for quality control for the activity related to the complaint or information.
- If the QC department receiving the complaint or information is not responsible, they must ensure the complaint or information is forwarded to the responsible person. Document the person to whom the complaint or information is forwarded to, and the date forwarded.
- Ensure all quality agreements specify responsibilities related to the handling of complaints.

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5. Is this the update to the Canadian GMPs that was originally expected to happen in March 2010?

Health Canada has incorporated recent regulatory amendments and clarification of existing requirements, including minor rewording and corrections, in addition to the EU standards for crimping that they had planned to make effective in March 2010.

6. When will Version 2 booklets be available?

Quality & Compliance Services Inc. will have booklets available as soon as possible. Current booklets are still useful; just add the following insert that lists the key changes.

GMP 2009 Edition Version 2	
Section	Change
C.02.013 Quality Control Department	Wholesalers now required to have QC department
C.02.015 Quality Control Department	<ul style="list-style-type: none"> • Additional detail regarding handling, communication and documentation of complaints • QA Agreements must specify responsibilities related to handling of complaints • Broadening of complaints to include “any information respecting the quality of a drug or its deficiencies or hazards”
C.02.024 Records	Validation of electronic systems for creating, modifying or storing records
C.02.029 Sterile Products, Manufacturing Control	<ul style="list-style-type: none"> • Additional detail regarding regular particulate and viable monitoring in Grades A and B areas • New interpretations pertaining to crimping requirements
Appendix B Glossary of Terms	New definitions for: <ul style="list-style-type: none"> • Grade A Air Supply • Quality Control Department Revised definitions for: <ul style="list-style-type: none"> • Drug Dilute Premix • Drug Establishment Licence • Drug Identification Number
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7. How can Q&C help me?

As your full-service partner for compliance, we can meet all of your GMP needs. We have solutions for your compliance challenges with:

- **Quality Control Officer (QCO) Services:** Our QCOs are fully qualified to assist or operate as your Quality Control department.
- **Validation Services:** We offer full validation services. Our specialists can help you with validation of procedures, computer systems, development of a compliance program to meet the temperature control requirements of GUI-0069, and any other validation activities.
- **Regulatory Services:** We can guide you through the Drug Establishment Licence process, DIN applications, and various Common Technical Document modules.
- **Laboratory Services:** We can help you develop and maintain a cost-effective testing program to meet requirements for finished product testing where required.

Contact us now to request a proposal or to learn more about how
Quality & Compliance Services Inc. can help you with
EASIER COMPLIANCE

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Quality & Compliance Services Inc. (Q&C®) is based in Mississauga (Toronto), Ontario, Canada. Since 1994, Q&C has assisted clients with:
Large Compliance Project Consulting, Audits, Validation Services,
Quality Control Officer (QCO) Services, Technical Writing Services,
GMP Training, Regulatory Services, and Lab Services.

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Compliance™ is the Dietary Supplement and Natural Health Product
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