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GMP in the QC Laboratory and Analytical Method Validation

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GMP in the QC Laboratory and Analytical Method Validation

S. Byrn 1, Z. Ekeocha2, M. Hynes3, R. Ongosi4, K. Clase5

Abstract

This document aims to provide suggestions for course content to the team designing a GMP QC laboratory and analytical method validation course. This course is a 30-minute high-level overview that is part of the USP GMP course.

Introduction

The overall goals are:

- Grasp the fundamental principles of GMP in a QC Laboratory setup including ISO17025.
- Describe GMP principles in daily, routine pharmaceutical testing programs and activities;
- Recognize the importance of quality in a GMP environment;
- Appreciate the importance of documented evidence of analytical method validation.

Listed below are the contents of the three modules. It should be noted that this 30-minute course is, by necessity, a very high-level offering since a typical GMP laboratory would have hundreds of SOPs and Documents. The employees of such labs would have advanced degrees in Pharmaceutical Sciences or Analytical Chemistry and have extensive training in analytical chemistry as well as good manufacturing processes and documentation. Because of this, this course provides a high-level overview of GMP in the QC laboratory. This would not be sufficient to ensure competency for the successful operation of a GMP QC laboratory and a successful Analytical Method validation. Future courses in a typical capacity building program or master’s degree program would address each modular topic in much more detail, with perhaps many lectures with discussion, quizzes, and case studies.

Module 1. GMP for Compliance QC (10 minutes)

Learning Objectives:

- Grasp the basic principles for the regulatory guidelines and quality standards (such as ISO 17025) applicable to QC laboratories’ requirements;
- Appreciate the basic principles of GMP in a QC Laboratory setup;
- Describe GMP principles in daily, routine pharmaceutical testing programs and activities;
- Describe the importance of quality in a GMP laboratory environment;
- Describe the importance of documented evidence and SOPs in a GMP laboratory environment, including the relevance for analytical method validation

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Content:

- Introductory slide with bullets describing each of the learning objectives

<table>
<thead>
<tr>
<th>Lesson</th>
<th>Topics</th>
<th>Main Elements of Slides</th>
</tr>
</thead>
</table>
| Lesson 1 | Regulations and Requirements overview – laws, regulations, and guidelines | • Founding of USP
• FDA laws, 1906, 1937, 1963
• GMP Law 1978 |
| Lesson 2 | Analytical Method validation/verification GC<1025><1026> | • Validation of Analytical Methods and procedures
• USP general chapters on analytical method validation
• ICH guidances
• FDA guidances
• Example Dissolution (including HPLC) |
| Lesson 3 | Calibration and qualification of lab equipment GC<1058> | • IQ/OQ/PQ of Instrument/equipment use in the laboratory
• Example HPLC |

Detailed Content:

- Figures for FDA Laws or Foundation of FDA
- Regulations and Requirements
  - Importance of proving methods is suitable for their intended purpose
- History and Founding of USP
  - Need for digitalis to have the same potency throughout the US colonies
- Founding of the FDA
  - 1906 – Purdue Professor Harvey Wiley, first FDA commissioner
  - 1937 – Sulfonamide elixir scandal
  - 1962 – Thalidomide
  - 1978 – GMP law with 8 systems
    - Figure showing timeline
- Analytical Method Validation and Verification
  - ICH Q2 – Validation of methods – mostly HPLC
    - Add guidelines for validation here
  - ICH Q14 Analytical Procedure Development
    - Knowledge and risk management
  - ISO 17025 – another way for QC laboratories to achieve international recognition
  - USP general chapters and other regulatory guidance e.g., FDA
  - Example of Dissolution Method Validation (HPLC Method)
    - Establish a validation protocol
    - Dissolution equipment selection
Module 2. Laboratory Compliance (10 minutes)

Learning Objectives:
- Describe the importance of regulatory guidelines and quality standards (such as ISO 17025) applicable to analytical laboratories requirement;
  - Possibly show timeline of GMPs, Six systems, and ISO 17025
- Describe the basic principles of GMP in a QC Laboratory setup;
- Describe the basic principles for the regulatory guidelines and quality standards (such as ISO 17025) applicable to QC laboratories' requirements;
- Describe the basic principles of GMP in a QC Laboratory setup;
- Explain GMP principles in daily, routine pharmaceutical testing programs and activities;
- Describe the importance of quality in a GMP laboratory environment

Content:
- Introduce module with slide with bullets covering module learning objectives.

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<th>Topics</th>
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<td>Master Plan</td>
<td>• Structure of QS</td>
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<td>• Necessity of a QS</td>
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<td>• Integrating QS with GMP controls</td>
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<tr>
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<td>• Elements of a Qs</td>
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<td></td>
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<td>• Overview of GMP in QC</td>
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<td>Lesson 2</td>
<td>Document Control</td>
<td>• Good documentation practices</td>
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<td>• Handling notebooks</td>
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<td>• Instrument quality systems</td>
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<td>Lesson 3</td>
<td>Internal Audit</td>
<td>• Overview of an internal audit</td>
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<td>• Conduct during an audit</td>
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<tr>
<td>Lesson 4</td>
<td>Sample Management</td>
<td>• Control of materials for testing</td>
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<tr>
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<td>• Bar code systems</td>
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<td>• Manual systems</td>
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<td>• Avoiding mix-ups</td>
</tr>
</tbody>
</table>
Detailed Content

- Various/different regulatory guidelines and quality standards (such as ISO 17025) apply to analytical laboratories' requirements.
  - Mention FDA, ICH, and ISO 17025, including management requirements and technical requirements.
  - Mention the importance of minimizing nonconformities
  - Mention strategies of following GMP to reduce nonconformities in a wide range of jobs in the QC laboratories
- A Master Plan is very important and guides overall laboratory compliance
- The basic principles of GMP in a QC Laboratory setup include
  - Laboratory procedures
  - Testing methods
  - Validation of methods
  - Addressing non-conformities
  - Stability studies
- GMP principles in daily, routine pharmaceutical testing programs and activities include specifications
  - Insert specifications table
- Recognize the importance of quality in a GMP environment;
  - Major quality train wrecks, including data integrity and shadow laboratories
  - Consider showing an image of the book – Bottle of Lies
- Recognize the importance and documented evidence of analytical method validation
  - Major train wreck including two sets of lab books and utilization of notes
- Document Control is critical for the QC lab
  - Show example of bad documentation
- Internal Audit can assist with discovering and resolving issues
- Sample Management
  - Importance of avoiding sample mix-ups and mislabeling/ chain of custody

Module 3. Quality System (10 minutes)

Learning Objectives

- Grasp the basic principles for the regulatory guidelines and quality standards (such as ISO 17025) applicable to QC laboratories' requirements;
- Appreciate the basic principles of GMP in a QC Laboratory setup;
- Describe GMP principles in daily, routine pharmaceutical testing programs and activities;
- Describe the importance of quality in a GMP laboratory environment;
- Describe the importance of documented evidence and SOPs in a GMP laboratory environment and for analytical method validation

<table>
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<tbody>
<tr>
<td>Lesson 1</td>
<td>Quality Manual</td>
<td>• Overview of a Quality Manual</td>
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</tbody>
</table>
| Lesson 2 | Data integrity - GDP | • Data integrity elements  
• Data integrity train wrecks |
| Lesson 3 | Investigation - CAPA | • OOS results  
• Deviations  
• CAPA |
| Lesson 4 | Supplier | • Lab suppliers  
• Supply chain issues for QC laboratories |
| Lesson 5 | Quality risk management | • Risk identification  
• Risk communication  
• Risk assessment  
• Risk management |

**Detailed content**

- Various/different regulatory guidelines and quality standards (such as ISO 17025) apply to analytical laboratories' requirements. Because of recent developments, the ICQ guidelines are among the most important, along with the extensive information in the USP general chapters.
- The basic principles of GMP in a QC Laboratory setup are clearly outlined in the ICH Q guidelines and the USP General Chapters and apply to daily, routine pharmaceutical testing programs and activities;
  - Show figure of ICH Q guidelines
- The laboratory measurements lack credibility without a strong quality system and analytical method validation.
- Describe how calibration is sued in the quality system.
- A Quality Manual organizes the entire laboratory QC system, providing an overview of the system and its organizational structure. The quality manuals should address all important aspects of a quality control lab, including facilities and equipment, document control, specifications, methods, validation, reference standards, training, change control, deviations, OOS, CAPA, data integrity, and stability.
- Data integrity is a critically important issue in the QC lab. It includes:
  - ALCOA – attributable, legible, contemporaneous, original, and accurate
  - Electronic Data handling systems, including LIMS systems or strong manual systems
    - Provide an example of LIMS system such as Labware, Elab
  - Training
  - Error management and audits
  - Data Archiving and Backup
- Investigations of deviations, OOS, and CAPA investigations are of major importance in a QC lab. As with many other topics in this module, an entire day-long short course could be devoted to this topic. Important steps in these activities include:
  - Initial assessment and investigation (Phase approach to investigations)
- Add risk diagram
  - Risk assessment
  - Action plan and corrective actions
  - Documentation
- Supplier and supply chain issues are assuming more importance and include
  - Add diagram of supply chain
  - Delays in shipment of critical equipment, repair parts, reagents, and reference standards
  - Information security and reliability
- Risk management includes the important steps of
  - Risk Identification
  - Risk communication
  - Risk assessment
  - Risk management

Additional text and relevant figures/diagrams could be adapted from the ICH guidance at [www.ich.org](http://www.ich.org).

**Acknowledgements**

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