QUALITY SYSTEMS APPROACH

FOR

CGMP IMPLEMENTATION – Philosophy to Practice

63rd IPC Bengaluru
17th December 2011

S.M. MUDDA
Micro Labs Limited
QUALITY SYSTEMS APPROACH FOR CGMP IMPLEMENTATION

CONTENTS:

1. WHY QUALITY SYSTEMS? - CURRENT ISSUES - GMPs & QMS

2. STRUCTURE & ELEMENTS OF PHARMACEUTICAL QUALITY SYSTEMS - PQS (US FDA, ICH Q10):

3. MANAGEMENT RESPONSIBILITY
   - PQS REQUIREMENTS
   - REGULATORY EXPECTATIONS
BACKGROUND:

Indian Pharma Industry - A Success Story

- In the recent years the Indian Pharmaceutical Sector has emerged as one of the world's leading and fastest growing markets.

- The industry has acquired a commendable position in the global pharma market as a supplier of high-quality, low-cost generic drugs.
BACKGROUND:
Indian Pharmaceutical Industry - A Success Story

A leading global provider already

- World’s 3rd largest generics producer
- Over US$ 8 Billion exports to 200 countries: 41% to U.S, EU & growing @ 20%+
- 179 USFDA,
- 84 MHRA;
- 153 EDQM;
- 814 WHO cGMP; &
- 49 sites have CEP Approved facilities
WHY QUALITY SYSTEMS?

Current Issues: GMPs & QMS

- Despite these accomplishments the Industry has many challenges-current as well as future.
- One such challenge is regulatory compliance: To remain in a state of on-going compliance with the regulatory requirements.
- We have had occasional unpleasant surprises when demanded to demonstrate an on-going compliance with the GMPs.
WHY QUALITY SYSTEMS?
Current Issues: GMPs & QMS

- Traditional approach towards product quality and GMP compliance do not encourage adoption of modern system-based approach.

QUALITY:
The sum total of the established **identity**, **strength**, **purity** + Other characteristics that have been designed to make a product **safe and effective**.

FUTURE DEFINITION: PRODUCT REALISATION!!
WHY QUALITY SYSTEMS?
Current Issues: GMPs & QMS

DETERMINATION OF QUALITY:

Product quality: Reliance on testing alone. Assurance of identity, strength and purity, however not of safety and efficacy.

OOS investigation: The tendency even today is to retest and retest until we get the desired results.
WHY QUALITY SYSTEMS?
Current Issues: GMPs & QMS

GMP: Focus only on need-based, risk-averse and inspection-oriented compliance.

- Success in inspection/approval of submissions.
WHY QUALITY SYSTEMS?

Current Issues: GMPs & QMS

- GMP as the name suggests is a practice
- Practices are followed by tradition.
- “How” of a practice is known while “why” is rarely known
- Accepting a practice without questioning is considered as compliance
WHY QUALITY SYSTEMS?
Current Issues: GMPs & QMS

- This also is largely due to our unwillingness to question seniors
- Status-quo gives a benefit of being comfortable with the existing practices
- Practices may not be uniform at different sites of the same company due to diverse backgrounds and cultural differences of the people
WHY QUALITY SYSTEMS?

Current Issues: GMPs & QMS

- The GMP regulations of different countries and their interpretation by the inspectors vary.

- How to comply with different requirements of the regulators and of the existing and the prospective customers at the same time??
WHY QUALITY SYSTEMS?

Current Issues: GMPs & QMS

- While adherence to GMP should ensure consistency, due to lack of uniformity of implementation, the good practices are seen to be inconsistently consistent.

- The industry needs to respond to this challenge with a paradigm shift in its approach towards GMP compliance.
THE WAY FORWARD

Adoption of QMS Approach

- It is time to look beyond the practices and understand philosophy or the concepts behind the practices.
- Practices without the support of the philosophy can never be implemented consistently and uniformly since the concepts teach us the reasons/purpose of each practice.
- Quality Management System (QMS) Precisely does this.
- The QMS serves as a structure/platform for implementation of GMPs.
THE WAY FORWARD -

The Pharmaceutical Quality System (PQS)

- US FDA realized this need and announced an initiative for 21st Century CGMPs in August 2002 with an intent to integrate Quality Systems and Risk Management approaches to meet the requirements of the agencies Current GMP Regulations (21 CFR Part 210 and 211).

QUALITY SYSTEMS APPROACH FOR CGMP IMPLEMENTATION

THE WAY FORWARD - PQS

US FDA INITIATIVE:

Five Guiding Principles:

- Risk-based orientation
- Science-based policies and standards
- Integrated Quality Systems orientation
- Internal cooperation
- Strong public health protection
THE WAY FORWARD - PQS

Overreaching philosophy of quality systems and GMP:
Quality should be built into the product, and testing alone cannot be relied upon to ensure product quality
The Quality System Model is organized according to the structure of international quality systems and the major sections of the model include the following:

- Management Responsibilities
- Resources
- Manufacturing Operations
- Evaluation Activities
The Quality Systems Model - US FDA

Six-System model: The Quality System provides the foundation for the five manufacturing systems that are linked and function within it.
QUALITY SYSTEMS APPROACH FOR CGMP IMPLEMENTATION

THE WAY FORWARD - PQS

The Quality System Model - US FDA:
Key Concepts of Modern Quality Systems used in the Guidance:

- Quality
- Quality by Design
- Quality Risk Management
- CAPA (Corrective and Preventive Action)
- Change Control
- Quality Assurance (The Quality Unit)
- Six-System Model
“Pharmaceutical Quality System ICH Q10” published in April 2009, recommended to enhance the quality and availability of medicines around the world, facilitate innovation and continual improvement and strengthen the link between pharmaceutical development and manufacturing.
QUALITY SYSTEMS APPROACH FOR CGMP IMPLEMENTATION
The three main objectives of the PQS compliment and enhance the compliance with the GMP requirements:

1. Achieve Product Realization:
   To establish, implement and maintain a system that allows the delivery of products with the quality attributes appropriate to meet the needs of patients, health care professionals, regulatory authorities (including compliance with approved regulatory filings) and other internal and external customers.
2. Establish and Maintain State of Control:

- Process Performance & Product Quality Monitoring System (PP&PQMS) for assurance of continued suitability and capability of processes.
- QRM can be useful in identifying the monitoring and control systems.
3. Facilitate Continual Improvement:
   To identify and implement appropriate
   • Product quality improvements,
   • Process improvements,
   • Variability reduction,
   • Innovations and
   • Pharmaceutical quality system enhancements,
   ➢ QRM can be useful for identifying and prioritizing areas for continual improvement.
PHARMACEUTICAL QUALITY SYSTEM - ICH Q10:

Important PQS Elements:

- Process Performance and Product Quality Monitoring System
- Corrective and Preventive Action
- Change Management
QUALITY SYSTEMS APPROACH FOR CGMP IMPLEMENTATION

PHARMACEUTICAL QUALITY SYSTEM - ICH Q10

What is Different?

- It is based on regional GMP requirements, ICH Q7 guideline “GMP for Active Pharmaceutical Ingredients” and has an ISO 9000 structure with a pharmaceutical context for terms and elements
- It facilitates the application of ICH Q8 & Q9.
PHARMACEUTICAL QUALITY SYSTEM - ICH Q10

What is Different?

- Regulatory requirements remain the same, anything in ICH Q10 is optional.
- GMPs provide guidance on most of the essential elements of a QMS but they lack detail on QRM. QRM has a larger focus in Q10.
- It has a life cycle focus starting from Development and includes Technology transfer, Commercial Manufacture and Product Discontinuation i.e. it links development and manufacturing.
PHARMACEUTICAL QUALITY SYSTEM - ICH Q10

What is Different?

GMPS:

- Address CAPA but not proactive continual improvement
- Do not address management responsibilities in detail
- Lacks detail on the management of outsourced activities
QUALITY SYSTEMS APPROACH FOR CGMP IMPLEMENTATION

Pharmaceutical Quality System Model

ICH Q10 Pharmaceutical Quality System

- Pharmaceutical Development
- Technology Transfer
- Commercial Manufacturing
- Product Discontinuation

GMP

Management Responsibilities

- Process Performance & Product Quality Monitoring System
- Corrective Action & Preventive Action (CAPA) System
- Change Management System
- Management Review

PQS elements

Enablers

- Knowledge Management
- Quality Risk Management
Management Commitment:

Senior Management has the Ultimate responsibility to ensure that an effective pharmaceutical quality system is in place.
Pharmaceutical Quality System : ICH Q10

Management Responsibilities:

1. Management Commitment:
   Management should:
   
   - Ensure timely & effective communication and escalation process to raise quality issues to the appropriate levels of management.
   - Define individual and collective roles, responsibilities, authorities, and interrelationships of all organizational units.
   - Conduct management reviews of process performance and product quality and of the pharmaceutical quality system.
Pharmaceutical Quality System : ICH Q10

Management Responsibilities:

2. Quality Policy:
   - Senior management should establish a quality policy that describes the overall intentions and direction of the company related to quality.

3. Quality Planning:
   - Senior management should ensure the quality objectives, to implement the quality policy, are defined and communicated.
QUALITY SYSTEMS APPROACH FOR CGMP IMPLEMENTATION

PHARMACEUTICAL QUALITY SYSTEM - ICH Q10

Management Responsibilities:

4. Resource Management:
   - Provide adequate and appropriate resources

5. Internal Communications:
   - Management should ensure appropriate communication processes are established and implemented within the organization.
PHARMACEUTICAL QUALITY SYSTEM : ICH Q10

Management Responsibilities:

6. Management of Outsourced Activities and Purchased Materials

- Assessing the suitability and competence prior to outsourcing
- Monitoring and review of the performance of the contract acceptor
- Monitoring incoming ingredients and materials to ensure they are from approved sources using the agreed supply chain.
PHARMACEUTICAL QUALITY SYSTEM : ICH Q10

Management Responsibilities:

Management Review:

Management Review Should Include:

- Periodic quality reviews, that can include:
  - a. Product quality complaints and recalls
  - b. PP and PQMS
  - c. Effectiveness of process and product changes including those arising from CAPA.

- Any follow-up actions from previous management reviews.
PHARMACEUTICAL QUALITY SYSTEM - ICH Q10

Management Review - Management should:

- be responsible for pharmaceutical quality system governance through management review to ensure its continuing suitability and effectiveness.

- assess the conclusions of periodic reviews of process performance and product quality and of the pharmaceutical quality system.
PQS - REGULATORY EXPECTATIONS:

Why do inspectors already look at an organization's QMS and QRM programmes during inspections?

- Looking at how companies react when things go wrong or are changing and are under pressure.
- Do they investigate to improve knowledge or simply build arguments for release of product?
PQS - REGULATORY EXPECTATIONS

Quality Management Findings - Investigations

- The quality of investigations performed was not of the required standard, with particular reference to....
- Complaints, rejects, deviations and out-of-specification data,
- Poor root cause Identification, Impact assessment and implementation of CAPAs
QUALITY SYSTEMS APPROACH FOR CGMP IMPLEMENTATION

PQS - REGULATORY EXPECTATIONS

- Appropriateness of depth of investigation
- Reactive rather than proactive usage of knowledge
- Quality is everyone’s responsibility- Is this true when things go wrong?
- Is the company a learning organization? And where is it on the learning curve?
PQS - REGULATORY EXPECTATIONS:
Quality Management Findings - Investigations

- Risk assessment and categorization were weak with the lowest impact risk appearing to be selected for every investigation.
- The change control system was not used despite a number of significant changes having taken place.
PQS - REGULATORY EXPECTATIONS:
So why these observations today in 2011?

- We all know having a good QMS is logical!
- Why would a sensible company not follow the elements of a robust QMS that are outlined in Q10?
- Inspectors know this, Regulatory Authorities know this, and Companies............?
PQS - REGULATORY EXPECTATIONS:

So when things start to go wrong what has happened?

- Management processes have failed!
- Risk identification may have failed! Resources?
- Identification and communication of emerging or changing risk may have failed!
- Investment in risk and quality management has failed!
- Knowledge management and the communication of the risk or changing risk has almost certainly failed!
- .........................and Senior Management has failed!
PHARMACEUTICAL QUALITY SYSTEM ICH Q10:

Benefits of Q10

- Provides top management commitment to Quality
- Enables transparency of systems, processes organisational and management responsibility
- Clearer understanding of the application of a Quality System throughout product lifecycle
PHARMACEUTICAL QUALITY SYSTEM ICH Q10:

What does Quality System success look like?

- Demonstrable signs of a true quality culture and quality leadership
- Price of non-conformance known and measured
- Processes mapped and well understood and monitored
- Tools such as lean and 6 sigma demonstrably in place
- Willingness to engage with regulators
- Above all - Management walk the talk
QUALITY SYSTEMS APPROACH FOR CGMP IMPLEMENTATION

SO WHAT DO WE NEED TO DO?....Change cultures!

- Change the culture to focus on the management aspects of quality rather than adherence to practices alone- Philosophy to Practice.
- Decision-making processes with product & process knowledge and risk management tools
- Redefine GMP as GOOD MANAGEMENT PRACTICE
- It is not necessary to change- survival is not mandatory! (W E Deming)
QUALITY SYSTEMS APPROACH FOR CGMP IMPLEMENTATION

ACKNOWLEDGEMENT

MR. R.S. IYER

The Quality Guru of the Indian Pharma Industry who taught me that

“QUALITY OF WORK DETERMINES THE QUALITY OF PRODUCTS”
QUALITY SYSTEMS APPROACH FOR CGMP IMPLEMENTATION

THANK YOU FOR YOUR ATTENTION

S.M. MUDDA
Executive Director - Technical & Operations
MICRO LABS LIMITED
NO.27, RACE COURSE ROAD
BANGALORE - 560 001
Mobile:+919972029070
smm@microlabs.in