Medical device QMS/GMP system and audit

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Pharmaceuticals and Medical Devices Agency
Office of GMP/QMS Inspection
Member GHTF SG3
Overview of presentation

QMS requirements

Establishment of QMS

Guidelines
- ISO Documents
- GHTF SG3 Documents
  etc..

QMS inspection

PMDA
NB
FDA
QMS Ordinance

Ministerial Ordinance on Standards for Manufacturing Control and Quality Control for Medical Devices and In-vitro Diagnostics (MHLW Ministerial Ordinance No.169, 2004)
Comparison of QMS Ordinance with ISO13485:2003

QMS Ordinance
- Seihin Hyojun Sho (Paragraph 2 of Article 6)
- etc..

ISO13485:2003
- Quality Management System
- Management Responsibility
- Product Realization
- Measurement, Analysis and Improvement

- Regulation of Biological-origin Medical Device, etc. Manufacturers (Article 73 to 79)

Substantially harmonized to ISO13485: 2003
Seihin Hyojun Sho
(Product Standard Code)

The manufacturer shall establish and maintain the document defining the product specifications and QMS requirements (Seihin Hyojun Sho), or identifying Seihin Hyojun Sho.

(QMS Ordinance Article 6 Para 2)
Seihin Hyojun Sho and ISO Documents

QMS Ordinance requires that the manufacturer shall establish and maintain the document defining the product specifications and QMS requirements (Seihin Hyojun Sho), or identifying Seihin Hyojun Sho. (QMS Ordinance Article 6 Para 2)

Seihin Hyojun Sho can be substituted by ISO documents if the relationship between Seihin Hyojun Sho and ISO documents is clearly identified.
MHLW Notifications

May 30⁰, 2011 Administrative Notice
  ⋅⋅⋅The relationship of QMS ordinance and ISO13485:2003
September 9⁰, 2005 Administrative Notice
  ⋅⋅⋅Tentative translation of QMS ordinance
March 30⁰, 2005 Notification No. 033001
  ⋅⋅⋅guidance document of QMS ordinance requirements
Overview of presentation

QMS requirements

Guidelines
- ISO Documents
- GHTF SG3 Documents
- etc..

Establishment of QMS

QMS inspection

PMDA  NB  FDA
Role of GHTF SG3

“SG3 is responsible for the task of examining existing quality system requirements in countries having developed device regulatory systems and identifying areas suitable for harmonization.”

www.ghtf.org/sg3/
<table>
<thead>
<tr>
<th>Title</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>SG3/N17/2008</td>
<td>Quality Management System - Medical Devices - Guidance on the Control of Products and Services Obtained from Suppliers</td>
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<tr>
<td>SG3/N18/2010</td>
<td>Quality Management System - Medical Devices - Guidance on corrective action and preventive action and related QMS processes</td>
</tr>
</tbody>
</table>

www.ghtf.org/sg3/sg3-final.html
Implementation of Risk Management Principles and Activities within a Quality Management System

GHTF SG3 Documents

GHTF/SG3/N15: 2005

FINAL DOCUMENT

Title: Implementation of risk management principles and activities within a Quality Management System

Authoring Group: GHTF Study Group 3

Endorsed by: The Global Harmonization Task Force

Date: May 20, 2005

Abrao Carvalho, GHTF Chair

This document was produced by the Global Harmonization Task Force, a voluntary international group of representatives from medical device regulatory authorities and trade associations from Europe, the United States of America (USA), Canada, Japan and Australia.

The document is intended to provide non-binding guidance to regulatory authorities for use in the regulation of medical devices, and has been subject to consultation throughout its development.

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This document discusses and supports the implementation and integration of a risk management system within a medical device manufacturer's quality management system and provides practical explanations and examples.
Quality Management Systems - Process Validation Guidance
GHTF/SG3/N99-10

This process validation guidance is intended to assist manufacturers in understanding quality management system requirements concerning process validation and has general applicability to manufacturing (including servicing and installation) processes for medical devices. The guidance provides general suggestions on ways manufacturers may prepare for and carry out process validations.
Quality Management System – Medical Devices – Guidance on the Control of Products and Services Obtained from Suppliers

The document herein was produced by the Global Harmonization Task Force, which is comprised of representatives from medical device regulatory agencies and the regulated industry. The document is intended to provide non-binding guidance for use in the regulation of medical devices, and has been subject to consultation throughout its development.

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The purpose of N17 is to provide good guidance and examples on the type and extent of control a device manufacturer could impose on its suppliers of a part or service. Guidance provided in the context of an effective ISO 13485:2003 quality management system.

**EXAMPLES OF OBJECTIVE EVIDENCE**

1. Identification of product and services
2. Specifications, part requirements, procedures, work instructions
3. Name and contact information of potential suppliers
4. Documented list of the risks identified
5. Documented process/product controls for manufacturer and supplier
6. Technological and operational capabilities, logistics, quality, technical risks
7. Selection criteria for potential suppliers, decision rationale
8. Documented evaluation and selection criteria
9. Documented initial agreement(s)
10. Documents and records
11. Documented decision and rationale
12. Contracts, purchase orders, etc.
13. Acceptance procedures; purchasing requirements
14. Specifications and requirements
15. Records of review and acceptance
16. Receiving records
17. Inspection records
18. Acceptance records
19. Records of results of any analysis of data
20. Records of any corrections
21. Manufacturer and/or supplier correspondence
22. Documentation and records of corrective and preventive action process

*This box delineates activities that can identify problems with the supplied product/services as well as supplier problems associated with adherence to the supplier arrangements.*

**GHTF/SG3/N17:2008**

Note: The depicted activities in this figure are not meant to be strictly sequential. In certain cases they may also occur in parallel.
Quality management system – Medical Devices – Guidance on corrective action and preventive action and related QMS processes
Provides guidance for establishing adequate processes for measurement, analysis and improvement within the Quality Management System (QMS) as related to correction and/or corrective action for nonconformities or preventive action for potential nonconformities of systems, processes or products.
Overview of presentation

Guidelines
- ISO Documents
- GHTF SG3 Documents
- etc..

QMS inspection
- PMDA
- NB
- FDA

QMS requirements
- QMS Ordinance
- ISO13485:2003
- 21CFR Part 820

Establishment of QMS

Continual improvement of the quality management system

Management responsibility
Resource management
Measurement, analysis and improvement
Product realization
Customers
Satisfaction
Input
Output
Requirements
Product
Types of QMS Inspections

Compliance inspection

1. Pre-approval inspection
2. Post-approval inspection (periodic inspection)

For - cause inspection etc.
## Compliance inspections

<table>
<thead>
<tr>
<th>Pre-approval Inspection</th>
<th>Post-approval inspection</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Based on application</td>
<td>• Based on application</td>
</tr>
<tr>
<td>• One of the requirements for marketing approval of medical device</td>
<td>• Conducted every five years after marketing authorization</td>
</tr>
</tbody>
</table>
## Authority of Compliance Inspection

<table>
<thead>
<tr>
<th></th>
<th>Domestic establishment</th>
<th>Foreign establishment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IVD</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New drug</td>
<td>PMDA</td>
<td>PMDA</td>
</tr>
<tr>
<td>Radioactive drug</td>
<td>PMDA</td>
<td>PMDA</td>
</tr>
<tr>
<td>Others</td>
<td>Prefectures (CB* for IVDs with certification standards)</td>
<td>PMDA (CB for IVDs with certification standards)</td>
</tr>
<tr>
<td><strong>Medical device</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New device</td>
<td>PMDA</td>
<td>PMDA</td>
</tr>
<tr>
<td>Cell/tissue derived device</td>
<td>PMDA</td>
<td>PMDA</td>
</tr>
<tr>
<td>Class IV</td>
<td>PMDA</td>
<td>PMDA</td>
</tr>
<tr>
<td>Class III</td>
<td>Prefectures</td>
<td>PMDA</td>
</tr>
<tr>
<td>Class II</td>
<td>Prefectures (CB* for medical devices with certification standards)</td>
<td>PMDA (CB for medical devices with certification standards)</td>
</tr>
<tr>
<td>Class I</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

CB: Certification body registered by Ministry of Health, Labour and Welfare
Compliance Inspections by PMDA

Target products (Medical devices and IVDs)
1. New medical devices, new IVDs
2. Cell-tissue-derived medical devices
3. Class IV medical devices
4. Radioactive IVDs
5. Medical devices manufactured in foreign manufacturing sites
   (Mainly Class Ⅲ, Ⅳ)
On-site Inspection and Off-site Inspection

On-site inspection is conducted in order of priority based on:
1 complexity of manufacturing processes;
2 risk associated with the use of products;
3 results of the previous on-site inspections; and
4 previous nonconformity, recall, or the contents

ex. New medical devices, cell-tissue-derived medical devices, class IV medical devices
On-site Inspection

1. In principle, two inspectors must be involved.
2. In principle, for about three days.
3. Notify 3-6 weeks before the date of inspection.
4. Request for data 1-2 weeks before the date of inspection.
5. Inspection in order of priority.
## QMS inspection schedule (example)

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Item</th>
</tr>
</thead>
</table>
| 1    | AM   | 1. Opening meeting  
|      |      | (1) Greeting  
|      |      | Confirmation on the audit schedule  
|      |      | (2) Opening of the audit (declaration)  
|      |      | (3) Presentation about the company (Corporate, CRM, plant)  
|      |      | Presentation about the plant (Overview, Infrastructure, Main Equipments)  
|      |      | (4) Presentation about the product  
|      |      | 2. Overview of Quality Management System  
|      |      | (1) Quality Manual  
|      |      | (2) QMS Organization  
|      |      | Document Structure  
|      |      | (3) Agreement with MAH  
|      |      | 3. Management Responsibility  
|      |      | (1) Quality Policy and Quality Objective  
|      |      | (2) Management Review  
|      | PM   | 4. Plant tour  
| 2    | AM   | 5. Design control (incl. Risk Management)  
|      |      | Product Information Control-Seihin Hyojunsho  
|      |      | 6. Manufacturing Including incoming inspection relating to key components (capacitor, etc.)  
|      |      | • Product and Process Control  
|      |      | • Validation  
|      |      | • Product Identification and Traceability  
|      |      | 7. Control of Monitoring and Measuring Devices  
|      | PM   | 8. Control of Nonconforming Product  
|      |      | 9. Training  
|      |      | 10. Purchasing Control (Control of Suppliers and Materials)  
| 3    | AM   | 11. Internal Audit  
|      |      | 12. CAPA  
|      |      | • Recall and Adverse Event  
|      | PM   | 13. PMDA wrap-up  
|      |      | 14. Confirmation on findings (Site Quality Director)  
|      |      | 15. Closing meeting (Site management representative)  

*Timeframe and items are subject to change depending on progress.*
Thank you ..

PMDA Website
http://www.pmda.go.jp/english/service/qms.html