Global Harmonization Task Force

Study Group 4 – "Regulatory Auditing"

Regulatory Auditing Strategy

Tim Missios, Vice Chair GHTF SG4**,**

Purpose of Study Group SG4

SG4 has been charged with the task of examining quality system auditing practices (initially among the founding members of the GHTF) and developing guidance documents laying harmonized principles for the medical device auditing process

Goals of GHTF SG 4

- Provide guidance for regulatory auditing of medical device manufacturers' quality systems
- Improve the effectiveness of regulatory audits
- Promote greater uniformity in the way regulatory bodies throughout the world conduct audits

SG 4 Current Membership

Active members consist of representatives from all founding members

CAs, CABs and industry representatives are present from Australia, Canada, Europe, Japan Taiwan and USA.

Chair of GHTF-SG 4 is Markus Zobrist – Swiss Medic

Secretary: Jan Welch – FDA

Vice chair: Tim Missios – Canadian Industry, MEDEC, Boston Scientific

New US Industry Member

SG 4 Current Membership

- U.S. (3)
  - Regulatory (2- **Secretary**)
  - Industry (1)
- Canada (2)
  - Regulatory (1)
  - Industry (1- **Vice Chair**)
- Australia (1)
  - Regulatory (1)
- Europe (7)
  - Regulatory (2 – **SG4 Chair**)
  - Notified Bodies (2)
  - Industry (3)
- Japan (4)
  - Regulatory (3)
  - Industry (1)

Structure of GHTF-SG4 "Regulatory Auditing" Documents

SG4 has developed / is developing a set of guidance documents dealing with:

Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers

– Part 1: General Requirements **(Status: Final)** + 4 Supplements **(Status: Final)**
– Part 2: Regulatory Auditing Strategy **(Status: Final)**
– Part 3: Regulatory Audit Reports **(Status: Final)**

Seven Final Guidance Documents developed by SG4

SG 4 Final Guidance

SG4(99) 28

Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers

Part 1: General Requirements

(updated Comment Period May 14, 2008)

General Requirements

- Written for auditing organizations
- May also be useful for manufacturers
- Provides guidance for establishing, planning, carrying out and documenting regulatory audits of quality systems
- Describes competence criteria for the audit team

SG 4 Final Guidance

SG 4(99) 14

Part 1: General Requirements

Supplement 1

Audit Language Requirements

Audit Language Requirements

- Purpose: To assure that auditors and the auditee are able to communicate clearly during an audit
- Before the audit, determine if auditors and auditee have a common language
- Arrange for an interpreter if there is no common language

SG 4 Final Guidance

SG4(00) 3

Part 1: General Requirements

Supplement 2

Training Requirements for Auditors

Training Requirements for Auditors

- The document describes training elements required to:
  - Prepare an individual to be an auditor
  - Qualify auditors to conduct regulatory audits of medical device manufacturers' quality systems
  - Maintain auditor qualifications

SG 4 Final Guidance

SG4 N(99) 24R3:

Part 1: General Requirements

Supplement No. 4

Compilation of Audit Documentation

Compilation of Audit Documentation

- Provides guidelines for compiling audit documentation within auditing organization for internal use
- This document does not address the exchange of audit documentation between auditing organizations

SG 4 Final Guidance

SG4-N26R1:2001

Part 1: General Requirements

Supplement No. 6

Observed Audits of Conformity Assessment Bodies

Observed Audits of Conformity Assessment Bodies

- Sets out guidance for observing audits conducted by Conformity Assessment Bodies (CABs).
- Observing audits enables a regulatory authority to evaluate the adequacy of the CAB's audits

SG 4 Final Guidance

SG4/N30 R 20: 2006

Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers

Part 2:

Regulatory Auditing Strategy

Regulatory Auditing Strategy

- Provides guidance on how to audit the effectiveness of quality systems in a systematic and effective manner within a reasonable time
- Purpose is to promote audit consistency – a necessity for harmonization and mutual recognition of audit results.

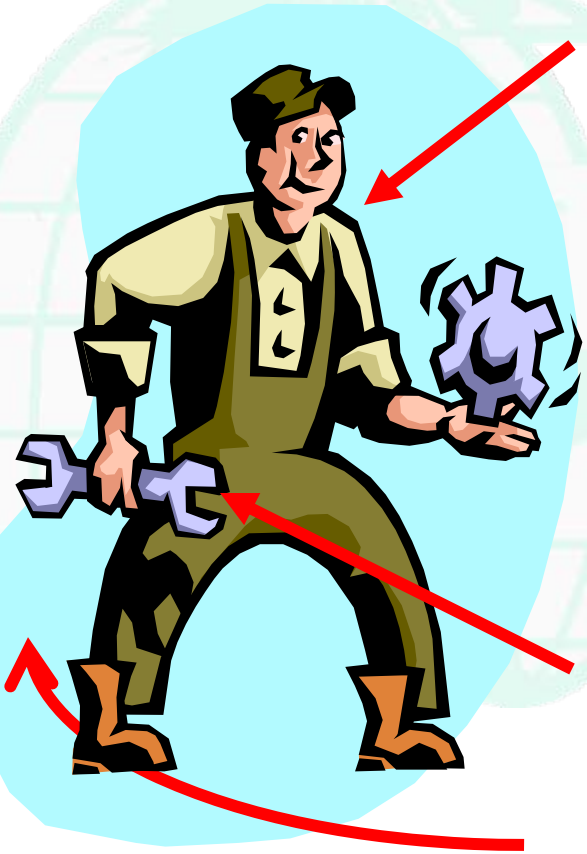
Topics

1. Does the process work?
2. How to demonstrate proper audit coverage?
3. Is Risk Management in place?
4. Conclusions

1. Does the process work

…according to the requirements of ISO 13485:2003 (QMS MEDICAL DEVICES)

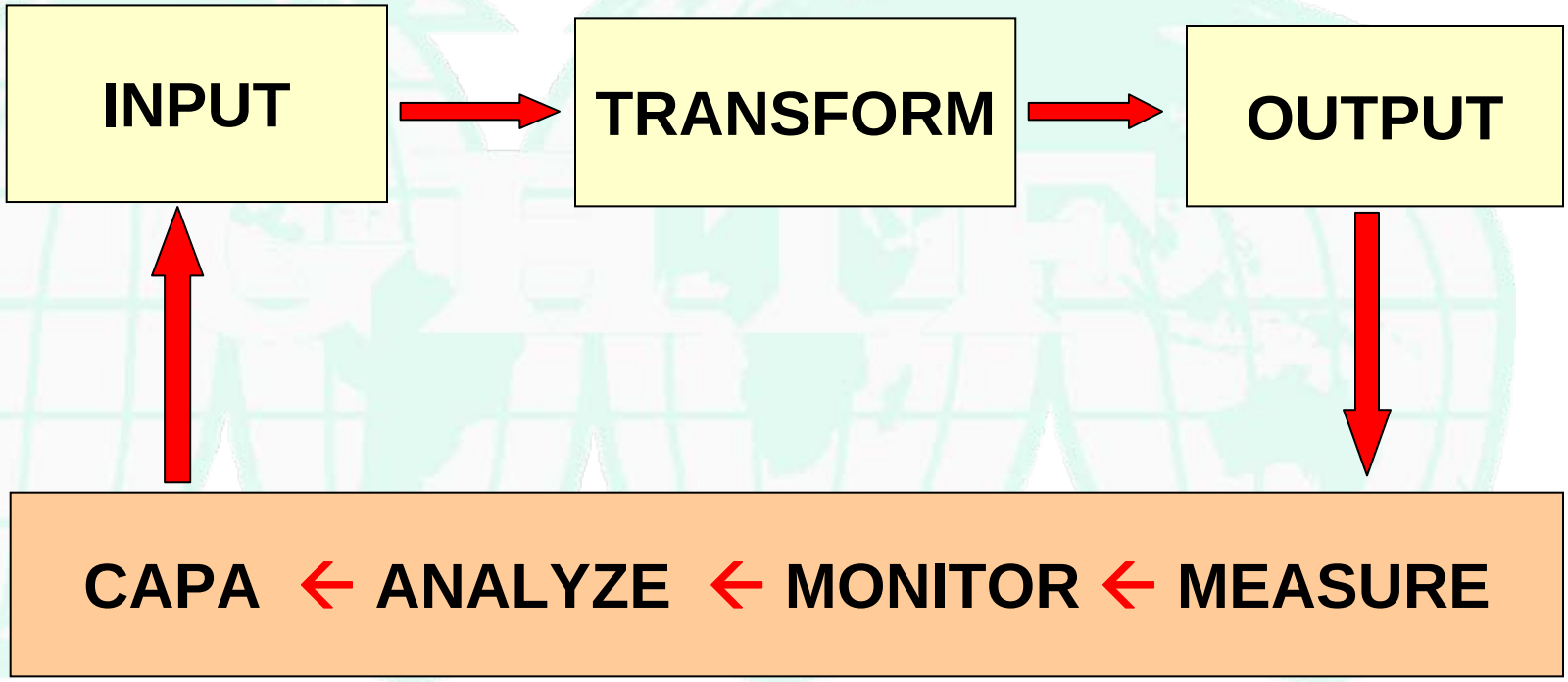
Attributes of a Process



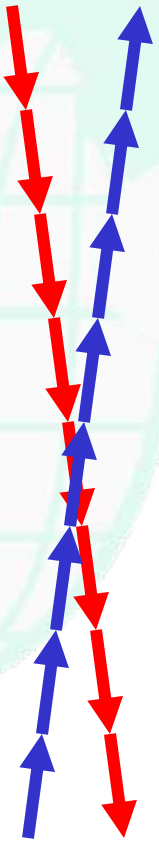
- PEOPLE
- METHODS
- MATERIALS
- MEASURES
- EQUIPMENT
- ENVIRONMENT

JW2E Development Method

Process Cycle



Process interactions

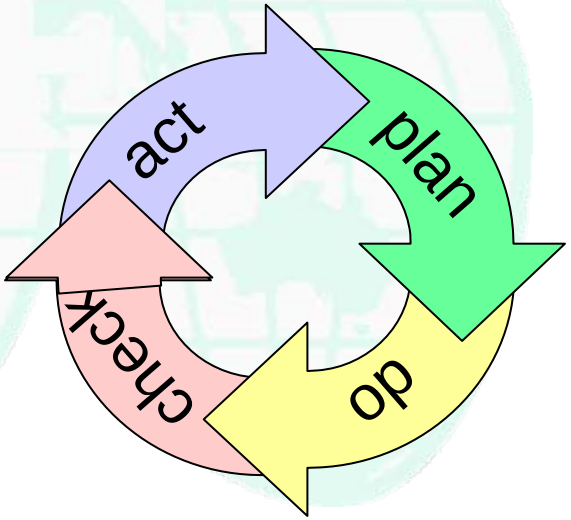


1. Management
2. Design and development
3. Product documentation
4. Production and process controls
5. Corrective and preventive actions
6. Purchasing controls
7. Documentation and records
8. Customer related processes

Process under control

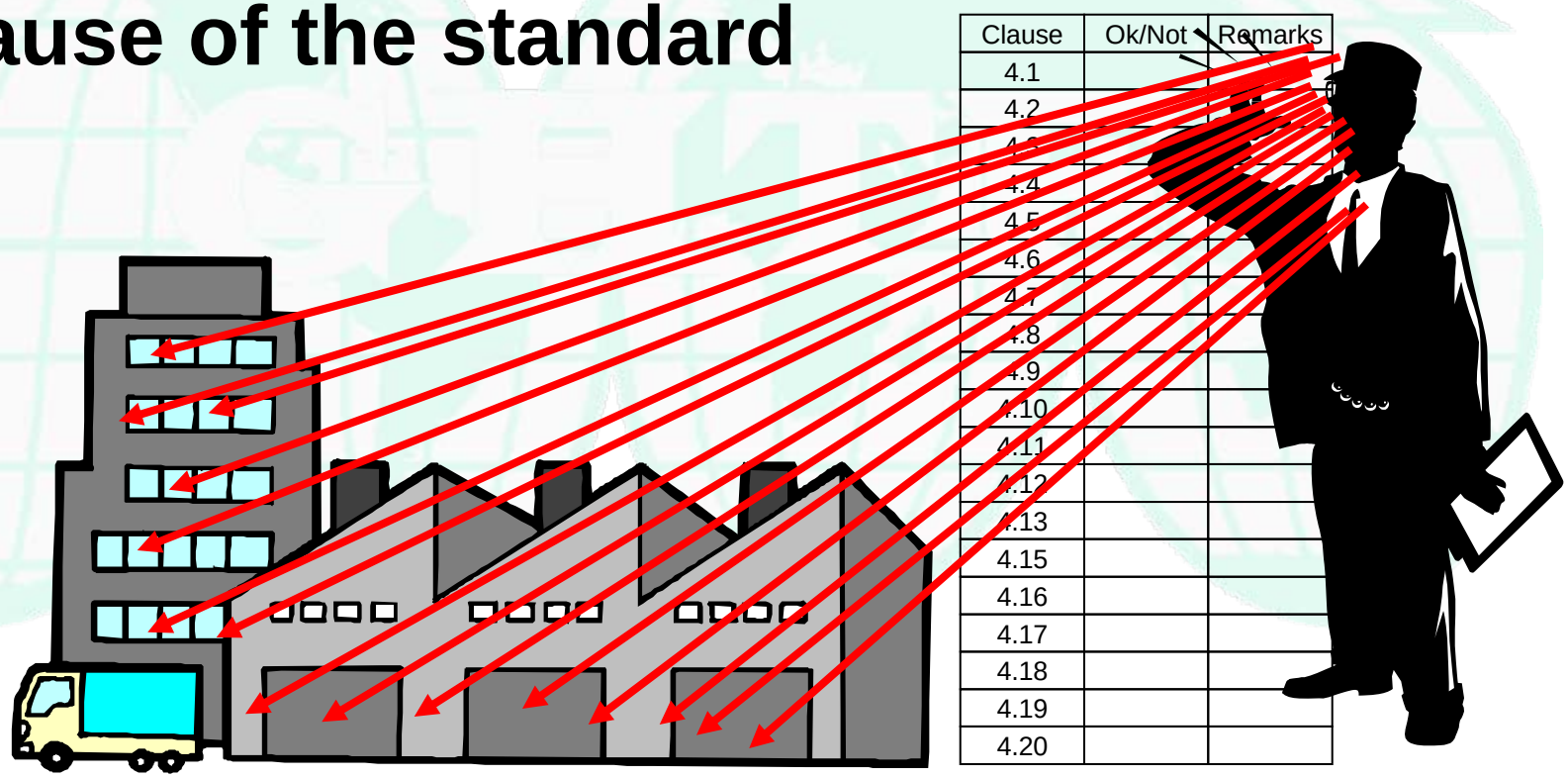
The process is unter control when the activity is

- Planned,
- Implemented,
- Measured &
- Action is taken!



2. How to demonstrate proper audit coverage

Good auditing practice in the past: Use of a checklist listing each individual clause of the standard

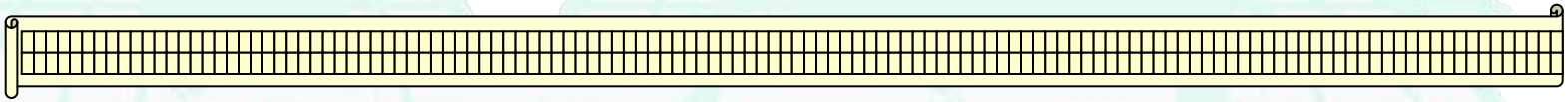


Audit challenge is increased: ISO13485:2003 – has 43 clauses!

- 7.5
  - 7.5.1
    - 7.5.1.1
    - 7.5.1.2
      - 7.5.1.2.1
      - 7.5.1.2.2
      - 7.5.1.2.3
    - 7.5.1.3
  - 7.5.2

The dilemma

- Can we or should we try and demonstrate clause coverage down to the lowest level?



- Or, will full clause coverage occur naturally if we follow the manufacturers' processes?
  - How can we prove it?
  - Will the regulators believe it?

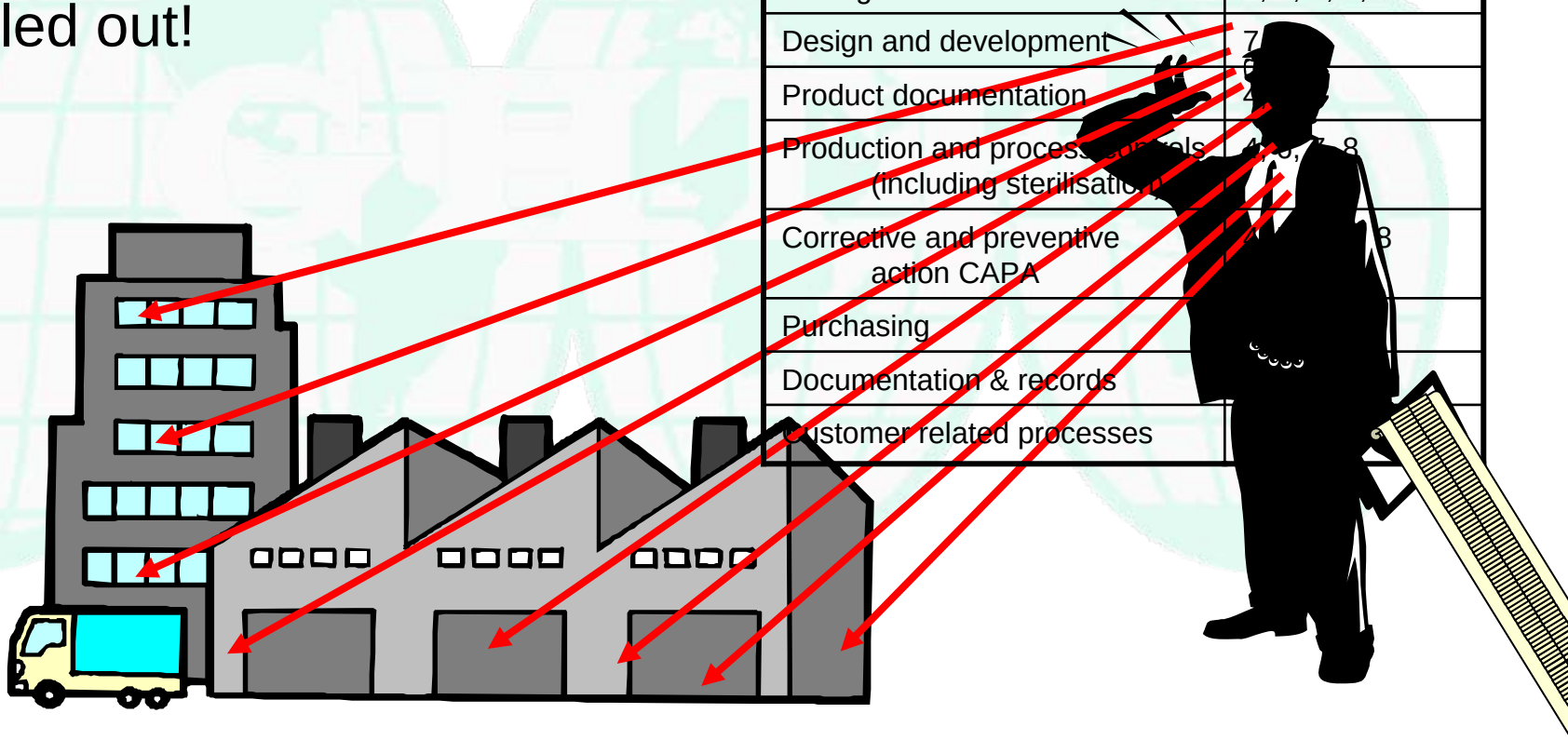
Auditing Subsystems

Subsystem	Clauses and subclauses of ISO 13485:2003
Management	4, 5, 6, 7, 8
Design and development	7
Product documentation	4, 7
Production and process controls (including sterilisation)	4, 6, 7, 8
Corrective and preventive action CAPA	4, 5, 6, 7, 8
Purchasing	7
Documentation & records	4
Customer related processes	7

State of the art is:

Use the subsystem approach for the audit even when finally a checklist needs to be filled out!

Subsystem	Clauses and subclauses of ISO 13485:2003
Management	4, 5, 6, 7, 8
Design and development	7
Product documentation	4
Production and process controls (including sterilisation)	4, 5, 7, 8
Corrective and preventive action CAPA	8
Purchasing	
Documentation & records	
Customer related processes	



3. Is Risk Management in Place

Risk Management Requirement in ISO 13485:2003

Section 7 Product realization

7.1 Planning of product realization

The organization shall establish documented requirements for risk management throughout product realization. Records arising from risk management shall be maintained.

NOTE 3 – See ISO 14971 for guidance related to risk management

Foundations

Product realization

Includes:

- Determination of customer requirements and customer communication (7.2)
- Design and development (7.3)
- Purchasing (7.4)
- Production and servicing (7.5)
- Control of monitoring and measuring devices (7.6)
- Delivery of the device

Foundations (cont'd)

ISO TIR 14969:2004

Medical devices – Quality management systems – Guidance for the application of 13485:2003

7.1.2 Risk management

Key elements of risk management include risk assessment (risk analysis and risk evaluation) and risk control

Foundations (cont'd)

Output of risk management activities can influence decisions and activities outside of product realization!

For example:

- management review decisions
- personnel training
- infrastructure
- monitoring and measurement
- handling of nonconforming product
- corrective and preventive actions
- …

Foundations (cont'd)

- **ISO 14971:2000**
  Medical devices – Application of risk management to medical devices

- **GHTF SG3 N15 R8:2005**
  Implementation of risk management principles and activities within a quality management system

Auditing a QMS

- **Risk management activities should be audited concurrently with the processes within the relevant subsystems**

- Purpose of auditing the risk management process is to ensure that adequate and effective risk management has been established and maintained through out the product realization process

- Can also assess the impact of the risk management process outputs on other areas of the QMS as mentioned in ISO TIR 14969

QMS Subsystems

1. Management
2. Design and development
3. Product documentation
4. Production and process controls
5. Corrective and preventive actions
6. Purchasing controls
7. Documentation and records
8. Customer related processes

Management Subsystem

- Verify that the product realization process incorporates risk management planning, and ongoing review of the effectiveness of risk management activities ensuring that policies, procedures, and practices are established for analyzing, evaluating and controlling risk

Management Subsystem

Auditor ...

- ☑ looks for statements in quality plan or quality manual that address the firm's approach to risk management activities
- ☑ reviews training records to determine if personnel are trained in risk management activities pertaining to their job
- ☑ determines if risk management principles are used in management reviews; are the outputs from these reviews risk-based?

Design and Development Subsystem

- Verify if products are by regulation subject to design and development procedures including risk management (e.g., hazard identification, risk evaluation and risk control)
- Verify that risk management activities are defined and implemented and that risk acceptability criteria are established and met throughout the design and development process
- Verify that any residual risk is evaluated and, where appropriate, communicated to the customer (e.g., labeling, service documents, advisory notices, etc.)
- It may be necessary to audit other subsystems to verify that risk acceptability criteria are met and residual risk is communicated if necessary

Design and Development Subsystem

- ☑Review risk analysis for a selected design project
- ☑Review design change control process procedures to determine integration of risk management principles
- ☑Select design changes for review and determine if re-evaluations were performed with respect to risk management activities

Product Documentation Subsystem

- For the product(s) selected verify that documentation includes (if required by national or regional regulations):
  - Risk management documents

☑Review technical file, design dossier, design history file, etc for this documentation

Production and Process Controls Subsystem

- Verify that the processes are controlled and monitored and operating within specified limits
- Verify that risk control measures identified by the manufacturer in production processes are controlled, monitored, and evaluated
- Verify that risk control measures are applied to delivery, installation, and servicing, where applicable
- Verify that the system for monitoring and measuring of products is adequate
- Ensure that any identified risk control measures are implemented

Production and Process Controls Subsystem

- ☑ Review validation protocol for a selected process and determine if risk management principles were used in determining key quality attributes for the process
- ☑ Determine if risk management principles were used to help establish appropriate monitoring techniques and frequencies
- ☑ Determine if risk management principles are applied to the evaluation of process changes, and the decision-making process for revalidation

Corrective and Preventive Actions Subsystem

When a CAPA results in a design change, verify that the hazard(s) and any new risks are evaluated under the risk management process.

- ☑ Are risk management principles used when deciding the scope of corrective and preventive actions? extended to similar processes or products?

- ☑ Review CAPA SOPs to determine degree of integration of risk management principles

Purchasing Controls Subsystem

Verify that the manufacturer assures the adequacy of specifications for products and services that suppliers are to provide, and defines risk management responsibilities and any necessary risk control measures

Purchasing Controls Subsystem

- ☑ Are decisions about suppliers based on risk management principles?
- ☑ Some suppliers may ship their components directly to stock, while other suppliers' components may undergo detailed acceptance activities at the manufacturer; are these differences based on risk management principles?
- ☑ Do supplier audits focus on risk management principles?

Customer Related Processes Subsystem

Confirm that customer feedback is analyzed in the product realization process and used to re-evaluate the risk assessment and, where necessary, adjust the risk management activities

- ☑ Is customer feedback evaluated in all appropriate QMS subsystems?
- ☑ Are all pertinent departments receiving the necessary information?
- ☑ Is customer feedback an input for risk management activities throughout the product realization process?

5. Conclusions

Subsystem Technique

- Regulatory auditing demands thorough and complete coverage
- Using the Subsystem technique is the current state of the art
- The Subsystem approach offers a solution to the problem of ensuring full coverage
- **and facilitates auditors to use a risk based approach for auditing**

Using the Subsystem Approach

- Leads to more efficient and effective auditing
- Leads to greater consistency in audit practices and feedback
- Increases the confidence in audit results

For benefit of

- the manufacturer
- the auditing organization
- the regulator

... and last but not least for the benefit of the patient!

SG 4 Final Guidance

SG4/N33 R 15

Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers

Part 3:

Audit Reports

Regulatory Audit Reports

- Scope
- Objectives
- User Needs of an Audit Report
- Main Points for a Regulatory Audit Report
- References for Applicable Documents

Regulatory Audit Reports

- Scope
  - used by regulators and auditing organizations as a guide for writing a report for a regulatory medical device QMS audit.
  - The regulatory audit report is a document or a set of documents from the audit team containing
    - Administrative data
    - A summary of locations
    - Functions or processes that were audited
    - Audit findings
    - Conclusions

Regulatory Audit Reports

- Objectives
  - The audit report comprises the documented evidence of a regulatory audit. It should contain sufficient information:
    - To document
      - The type of audit
      - The audit criteria
      - What was covered in the audit
      - The audit findings
    - To evaluate the manufacturer's
      - Compliance status
      - Effectiveness of the implementation of the QMS and draw audit conclusions
    - To allow for the exchange of audit reports between regulatory authorities/auditing organizations

Regulatory Audit Reports

- User Needs of an Audit Report
  - Auditing Organization/Regulator Perspective
  - Designating Authority Perspective
  - Manufacturer/Auditee Perspective

Regulatory Audit Reports

- Main points for a Regulatory Audit Report
  - The audit report is a traceable document(s) from the regulatory audit team
  - Reporting procedures should meet need of the auditing organization
  - Reporting procedures shall ensure all common data are included in their reports
  - The audit report shall be typed
  - The audit report shall be formatted so it can be stored and transferred electronically

Note: The language of the report should be agreed upon between the auditee and the auditing organization prior to the start of the audit.

Regulatory Audit Reports

- Main points for a Regulatory Audit Report
  - Data Concerning Auditee
  - Data Concerning Audit
  - Audit Trail
  - Conclusion
  - Signature and Dating of Report
  - Attachments (that could be used to support the content of the report)

Regulatory Audit Reports

- Main points for a Regulatory Audit Report – ***Signature and Dating of Report***
  - Date of the audit report
  - Lead auditor, auditor(s) names, titles and organizations
    - Signature and/or stamp of auditors on report

Regulatory Audit Reports

- References for Applicable Documents
  - GHTF/SG4/N28R2:
    - Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers – Part 1: General Requirements (1999)
  - GHTF/SG4/N30R18:
    - Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers – Part 2: Regulatory Auditing Strategy (final document 16 Feb 2006)
  - GHTF/SG2/N36R7:
    - Manufacturer's Trend Reporting of Adverse Events
  - US FDA 21CFR820:
    - Quality System Regulation
  - ISO 9000:2005:
    - Quality Management Systems – Fundamentals and Vocabulary
  - ISO 13485:2003:
    - Medical Devices – Quality Management Systems – Requirements for Regulatory Purposes
  - ISO 19011:2002:
    - Guideline for Quality and/or Environmental Management Systems Auditing

Next Steps…..

Ongoing Work

SG4(PD)/N28R3

Guidelines for Regulatory Auditing of Quality Management

Systems of Medical Device Manufacturers – **Part 1: General Requirements**

Comment period until May 14, 2006

Ongoing Work

SG4 (WD)N83 - Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers – Part 2: Regulatory Auditing Strategy, Supplement No. 1 Multi-site Audits and Audits of Suppliers

SG4 (WD)N84 - Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers – Part 2: Regulatory Auditing Strategy, Supplement No. 2 Auditing of Supplier Control.

Next Meetings

Paris, France - April 1-3, 2008

Canada, October, 2008

Additional Information……

Visit the GHTF website at: www.ghtf.org

– Website includes
  - Steering Committee & procedure documents
  - Study group guidance documents & membership
  - Discussions from past GHTF conferences
  - Upcoming meetings and strategic plan

Thank you!