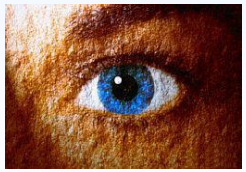
ISO 13485

Willem van den Biggelaar

Quality & Regulatory Consultant

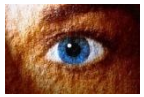
PROCESS VISION

DOWN TO EARTH QUALITY SERVICES



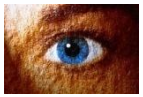
Content

- Let’s introduce ourselves
- What I want to tell
  - Why do you want/need ISO 13485
  - Scope of quality system
  - ISO 13485 versusr regulatory
  - Global difference with ISO 9001
  - Audit experiences
  - QMS architecture
  - ISO 13485 project approach
- Discussion



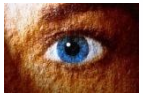
Process Vision – 25 years of experience

- DEKRA (previous KEMA) auditor for
  - ISO 9001
  - ISO 13485
  - CMDCAS (Canadian regulatory)
- Consultant on regulatory for medical devices
- Quality Assurance in development projects
- Some customers
  - Philips Healthcare
  - ASML
  - Frencken Mechatronics
  - Centre for Concepts in Mechatronics
  - DORC international
  - eventIS
  - Sintecs



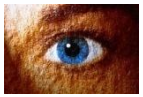
And now it’s your turn…….

- Name
- Function within organisation
- Legal manufacturer of medical devices?
- Supplier to legal manufacturer?
- Development?
- Production?
- ISO 9001 certified?
- Expectations of this meeting

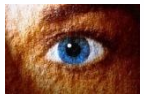


Why do you want ISO 13485?

- Is your customer pressing you?
  - E.g FDA has its targets set to the suppliers of the legal manufacturers of medical devices.
  - Legal manufacturers in return demand from suppliers to be ISO 13485 certified.
  - Advice: No questions asked, just implement 13485 but always keep thinking for yourself (do not blindly follow the customer)
- Do you want to bring medical devices to the market as a legal manufacturer?
  - Advice: ISO 13485 is a good start
- Do you want to improve your processes internally?
  - Advice: ISO 13485 will not really help, ISO 9001 is good enough or maybe CMMI?
- ISO 13485 is not a mandatory standard!
  - But auditors will be very annoying if you are not 13485 certified

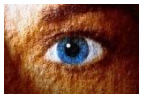


Scope of the Quality Management System (QMS)



Scope of your quality system

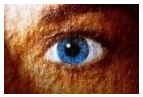
- Your medical product must comply to
  - regulatory requirements from the countries in which you sell your medical device. This is mandatory.
- These requirements differ per area, some examples
  - European Union:
    - MDD: Medical Device Directive 93/42/EEC
    - IVD: In Vitro Diagnostics medical devices 98/79/EC
    - AIMD: Active Implantable Medical Device Directive
  - USA: CFR: Code of Federal Regulations – E.g. 21 part 820 QSR (FDA)
  - Canada: MDR: Medical Device Regulations – SOR / 98 – 282
  - Japan: PAL: Pharmaceutical Affairs Law
  - Taiwan / China: similar to FDA



Scope of your quality system – part 2

- ISO 13485 has its roots in the European Union

- ISO 13485 will help you implement the national regulatory requirements for your products



To put it all in perspective

- You want to bring a medical product to the market

Or

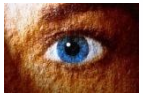
- You are supplier to a legal manufacturer who brings a medical product to the market

Then

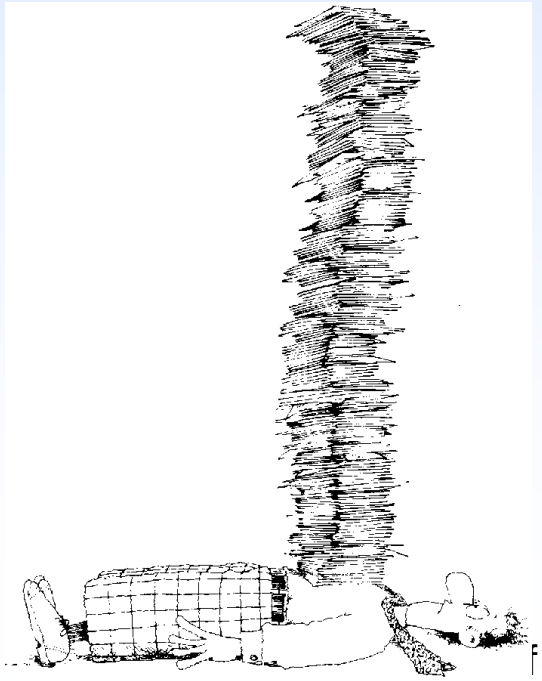
- Your product has to be compliant with national regulatory requirements.

And

- A international standard like ISO 13485 can help you to setup a quality system that supports adhering to these national regulatory requirements but does not cover it all.



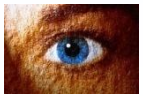
ISO 13485 in relation to regulatory



Coverage of European regulatory

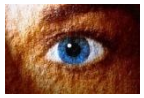
- MDD is covered mostly but not completely
- For example MDD demands
  - State of the art software validation (e.g. ISO 62304)
  - Reduce risk of use errors (e.g. IEC 62366)
  - Specific requirements for
    - Vigilance (near) Incident reporting & recalls
      - MEDDEV 2.12-1* for guidance
    - Post Market Surveillance: experience from post market production
      - MEDDEV 2.12* for guidance
    - Clinical Evaluations
      - MEDDEV 2.7.1* for guidance

*Google “MEDDEV” and you will find the guidance docs



Coverage of Canadian regulatory

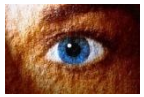
- MDR has ISO 13485 as backbone
- A few extra demands
  - More explicit labeling requirements
  - Explicit Software validation
  - Distribution records for all devices not only implantable
  - Specific requirements for
    - Complaints
    - Mandatory problem reporting (incidents)
    - Recalls



Coverage of USA regulatory

- FDA demands on top of Canadian MDR, e.g.
  - Include development in Software tool validation
  - Tool validation for electronic records / electronic signatures (CFR part 11)
  - Design Transfer is mandatory, for 13485 a guidance
  - Independent reviewers
  - Signatures for design input and output

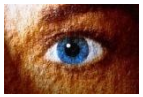
  - More info?
    The Quality System Compendium:
    GMP Requirements & Industry Practice (AAMI)



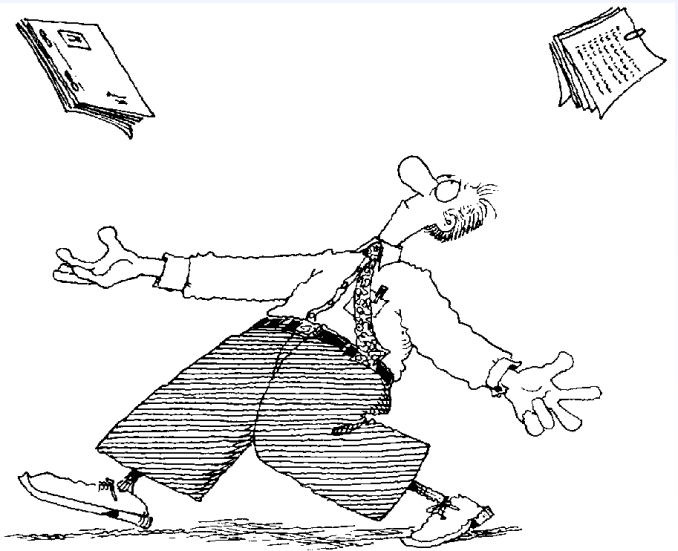
Harmonization among regulatory

- Global Harmonization Task Force (GHTF)
  - A partnership between regulatory authorities and regulated industry, the GHTF is comprised of five Founding Members: European Union, United States, Canada, Australia and Japan
- 5 study groups with helpful documentation
  - SG1: Pre market evaluation
    - Definitions / Labeling / Device Classification / Safety principle
  - SG2: Post Market Surveillance / Vigilance
  - SG3: Quality Systems
  - SG4: Auditing
  - SG5: Clinical Safety / performance

Google “GHTF” and you will find the guidance docs

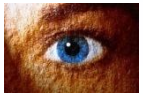


ISO 9001
versus
ISO 13485



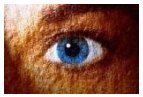
Difference with ISO 9001 in a nutshell

- No focus on customer satisfaction but on meeting customer and regulatory requirements
- No continual improvement model but maintain effectiveness of QMS
- Regulatory requirements are input throughout the system
- Maintain a Technical Dossier (TD) for each (group of) devices
- Risk analysis (patient safety) throughout the design process (ISO 14971)
- Clinical Validation (Evaluation) part of design validation
- Validation of software tools used in production / service
- Review before approve and after change of controlled docs
- More documented procedures & proof via records (see next sheets)



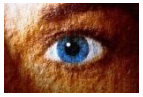
Criteria for QMS: always risk based

- Complexity of the product(s)
  - Blood transport bags with climate control
  - MRI scanner
- Size of company
  - 5 FTE of which 2 developers
  - 500 FTE of which 50 developers
- Example
  - 7.3.7 Control of design and development changes
    - Changes reviewed, verified, validated and recorded
    - Low risk: update of version history of document
    - High risk: change control board, change track tool



ISO 9001: 7 procedures

4.2.2	**Quality manual**
4.2.3	**Control of documents**
4.2.4	**Control of records**
8.2.2	**Internal audits**
8.3	**Control of nonconforming product**
8.5.2	**Corrective action**
8.5.3	**Preventive action**



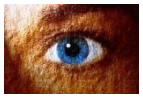
ISO 13485: 26 procedures

4.2.2	Quality manual
4.2.3	Control of documents
4.2.4	Control of records
6.2.2	Training (if required by regulations)
6.4	Work environment
7.3.1	Design & development planning
7.4.1	Purchasing process
7.5.1.1	Control of production and service provision
7.5.1.2.3	Servicing activities
7.5.2.1	Validation of computer software
7.5.2.2	Validation of sterile processes
7.5.3.1	Product identification
7.5.3.1	Returned product identification
7.5.3.2.1	Product traceability
7.5.5	Product Preservation
7.5.5	Product Preservation shelf-life and sp
7.6	Control of monitoring & measuring d
8.1	Statistical Techniques (if required by regulations)
8.2.1	Feedback system (post market surveillance)
8.2.2	Internal audits
8.3	Control of nonconforming product
8.4	Analysis of data
8.5.1	Issue & implementation of advisory notices
8.5.1	Notification of adverse events
8.5.2	Corrective action

ISO 9001: 22 record types

5.6.1	Management review
6.2.2 (e)	Competence, awareness & training
6.3	Maintenance
7.1 (d)	Planning of product realization
7.2.2	Review of requirements related to product
7.3.2	Design & development inputs
7.3.3	Design & development outputs
7.3.4	Design & development review
7.3.5	Design & development verification
7.3.6	Design & development validation
7.3.7	Control of design & development changes
7.4.1	Supplier evaluations

7.5.3.	Product traceability
7.5.4	Customer property
7.5.5	Preservation of product
7.6	Calibration (as found)
7.6	Calibration (corrected)
8.2.2	Internal audits
8.2.4	Product release authorisation
8.3	Nonconformances (nature)
8.5.2	Corrective action
8.5.3	Preventive action



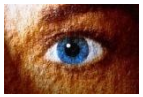
ISO 13485: 39 record types

5.6.1	Management review
6.2.2 (e)	Competence, awareness & training
6.3	Infrastructure Maintenance
7.1 (d)	Planning of product realization
7.1	Risk management
7.2.2	Contract Review
7.3.1	Design & development planning
7.3.2	Design & development inputs
7.3.3	Design & development outputs
7.3.4	Design & development review & actions
7.3.5	Design & development verification
7.3.6	Design & development validation
7.3.7	Design & development changes
7.3.7	Design Review change result
7.4.1	Supplier evaluations & actions
7.4.2	Purchasing information
7.4.3	Verification of purchased product
7.5.1.1	Batch records
7.5.1.2.2	Installation & verification activities
7.5.1.2.3	Servicing activities

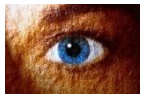
7.5.1.3	Sterilization parameters
7.5.2.1	Validation (process)
7.5.2.2	Validation (sterilization)
7.5.3.2.1	Product traceability
7.5.3.2.2	2 x: implantable / Consignee name & address
7.5.4	Customer property
7.5.5	Shelf-life and special storage
7.6	2 x: Calibration (as found & as corrected)
8.2.2	Internal audits
8.2.4.1	Product release authorisation
8.2.4.2	Implantable: Product inspection & testing
8.3	Non conforming product
8.4	Analysis of data
8.5.1	Customer complaints (investigations)
8.5.1	Customer complaints (no action)
8.5.2	Corrective action
8.5.3	Preventive action

Background information on ISO 13485

- ISO/TR 14969 Guidance on the application of ISO 13485
- Annex B of ISO 13485: difference between 13485 and 9001

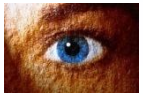


Audit
non compliance
examples



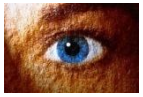
Audit NC examples: QMS / CAPA

- Non application of ISO 13485 has not been defined in the QMS.
- The quality policy is not communicated directly to the organization nor reviewed on a periodic basis.
- Control of improvement actions defined as a result from PPC meeting is not sufficient, for example: actions XXX were defined in 06/08 and are still open; due dates were not defined.
- No documented CAPA procedure available. Non conformities are not recorded as such.



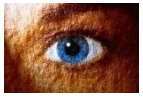
Audit NC examples: design and development

- No design reviews take place as required in the norm. At least one design review should take place during the project.
- Test specifications are not traceable back to development input requirements so it cannot be assured that the design output has met the design input.



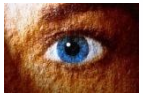
Audit NC examples: measuring devices

- 5 measurement devices are used for staging activity. The calibration date of the YY meter is expired with 2 months. The calibration status of the ZZ measure device is not verified due to an unreadable label.
- Within the organization, no responsible person is appointed for the calibration control of these measurement devices.



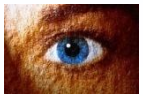
Audit NC examples: software validation

- A new software application was introduced to handle complaints and order handling; related to this software application:
  - A documented procedure for software validation is not available
  - Complaints are analyzed for trending, using the software application. Because the results could affect product quality, this part of the application must be validated.
  - No rationale is available which explains why the electronic complaint database application don’t require validation

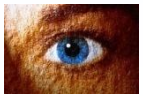


Audit NC examples: purchase

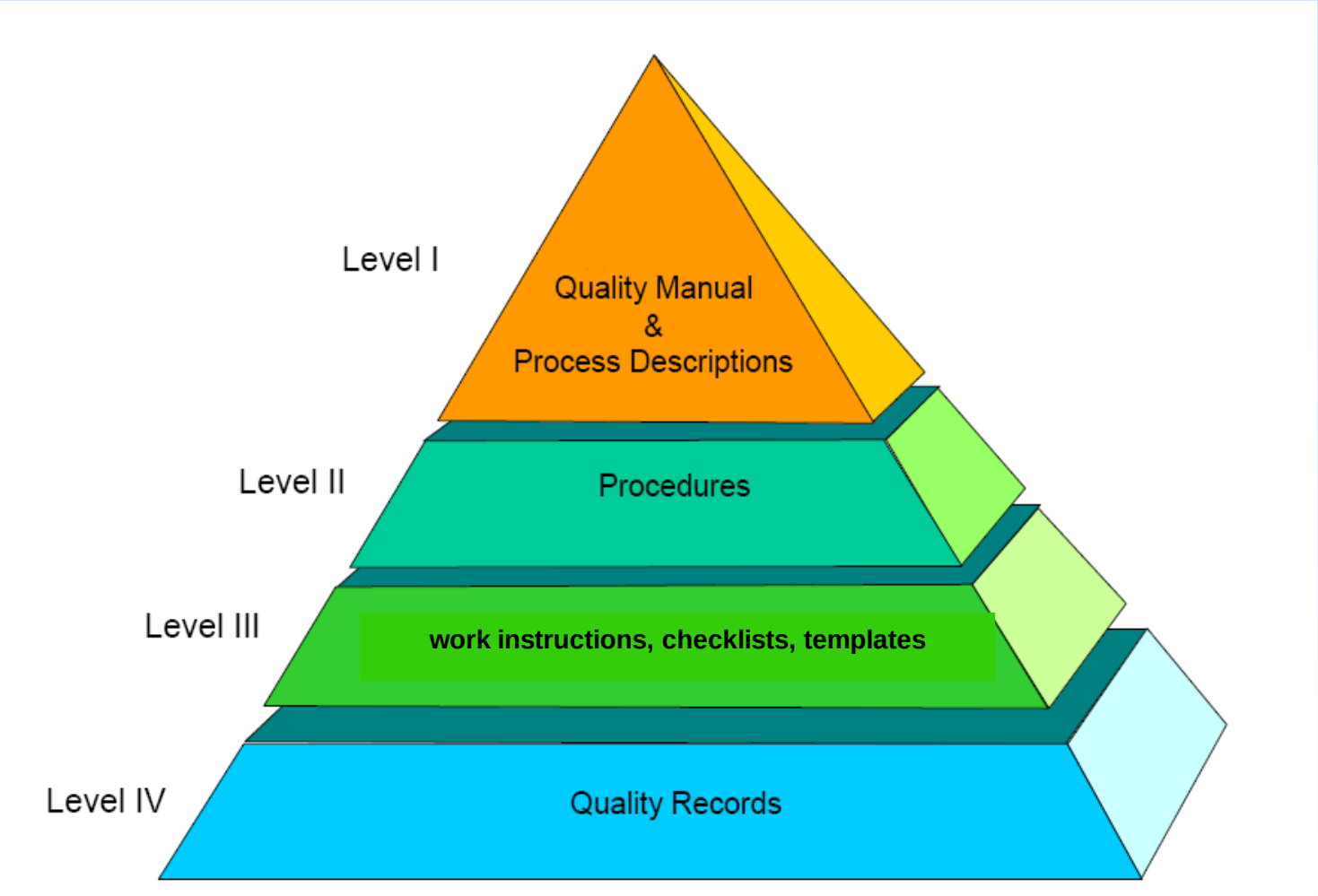
- No criteria for supplier selection, evaluation and re-evaluation are defined.
- Not all records related to supplier evaluation could be demonstrated, for example: suppliers XXXX and YYY, years 2007, 2006 and 2005.



QMS architecture

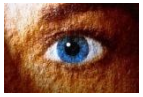


QMS architecture

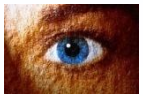


Possible content of Quality manual

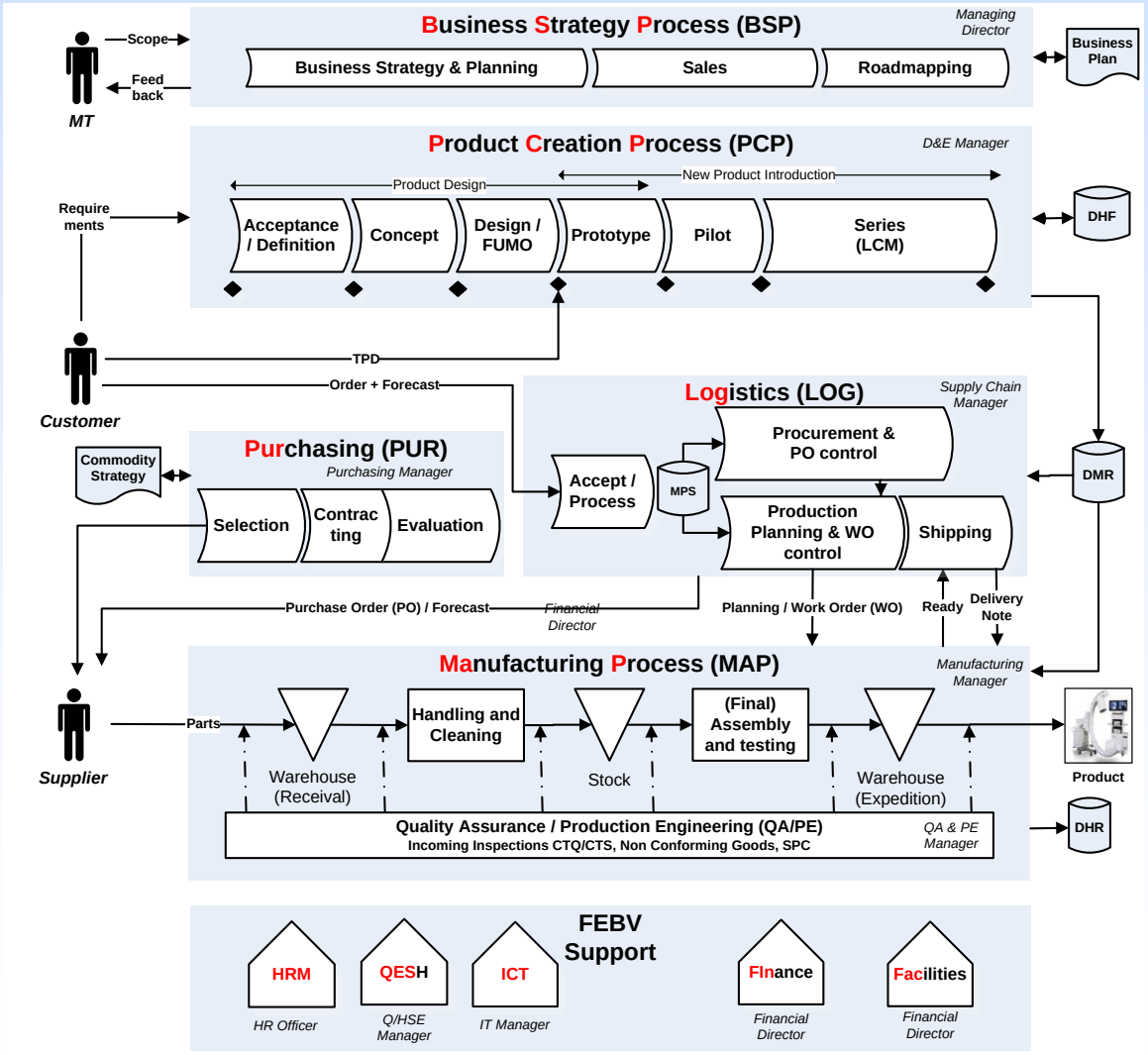
- Required according norm
  - Scope of QMS
  - Quality policy / objectives
  - Non application / exclusions with motivation
  - Processes with interaction
  - Reference to all procedures
  - Outline structure of documentation of QMS
- Organisation / product portfolio
- Strategy / mission / goals



Example of a Quality Manual

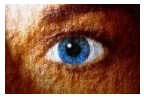


Identify your processes, example:

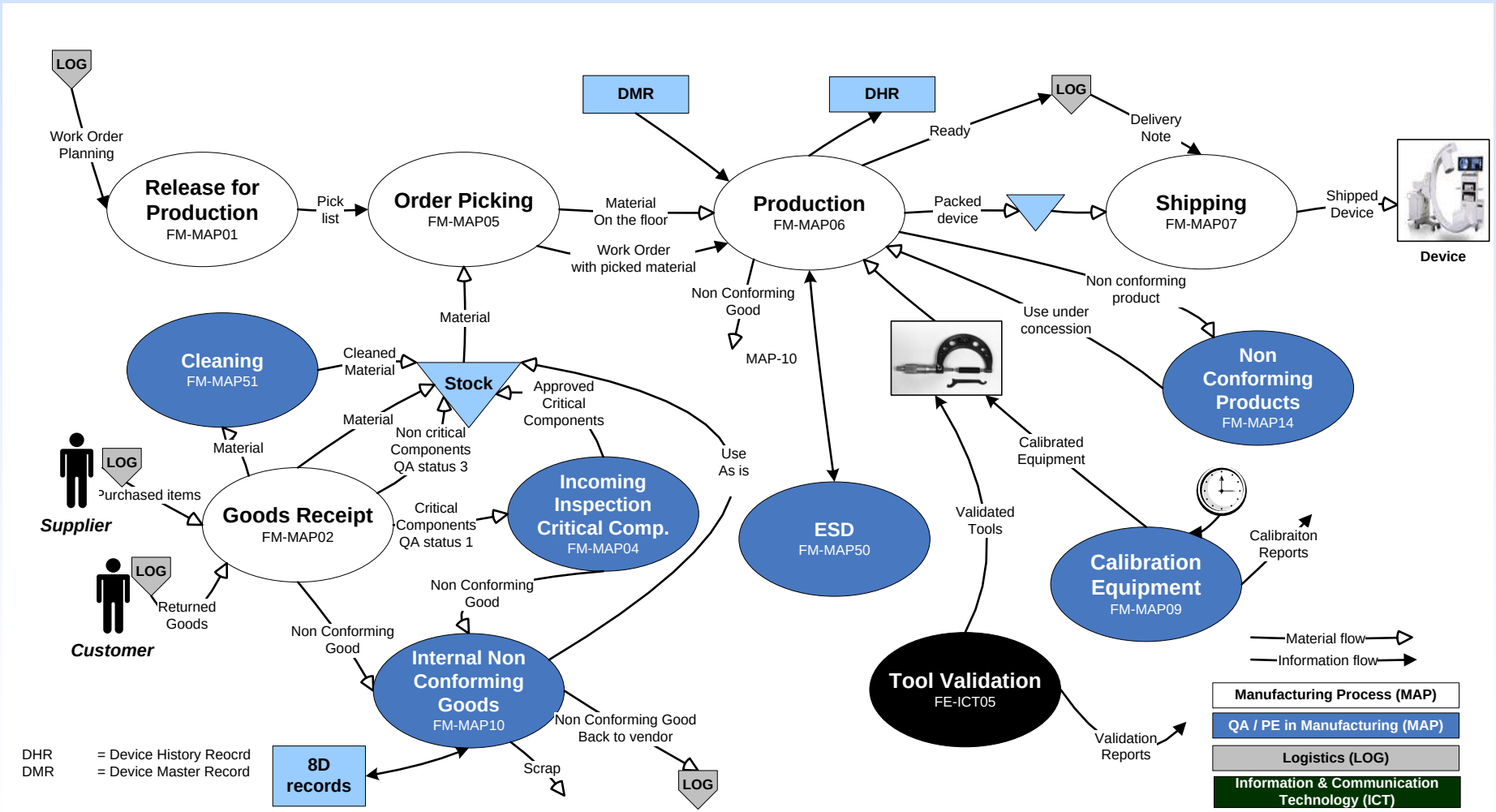


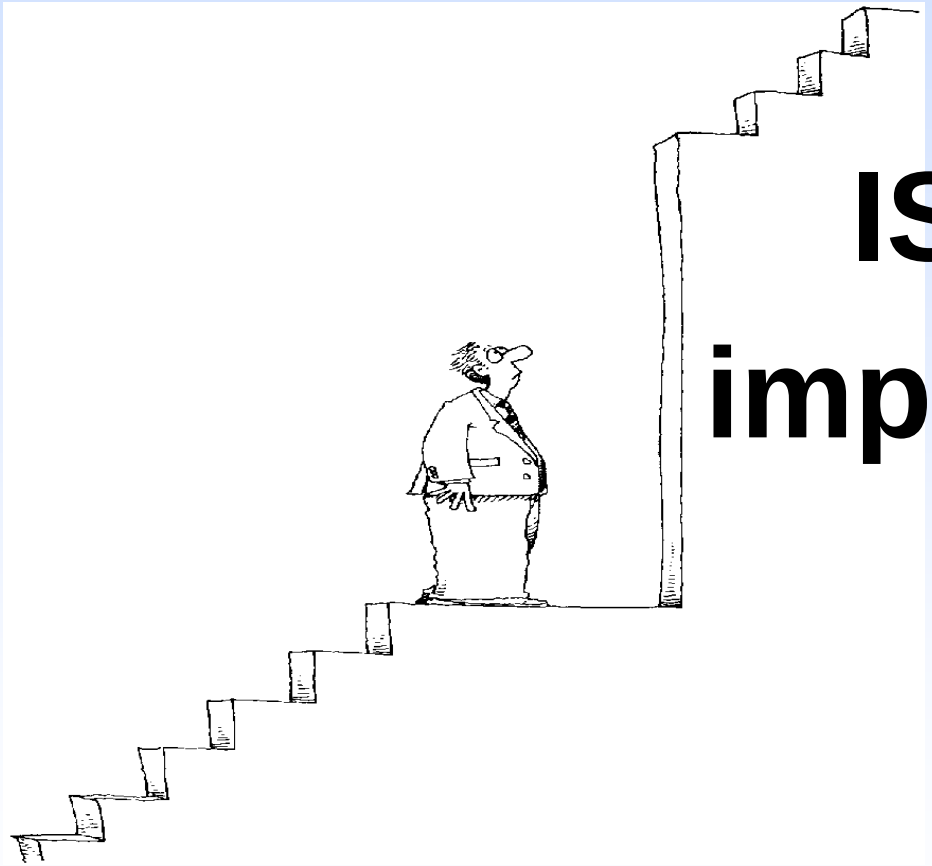
QMS procedure interfaces

- Gives insight in how system is build up
- Is useful for training purposes
- Can be used as view on the QMS



Example of procedure interface

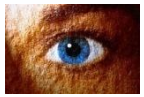




ISO 13485 implemenation

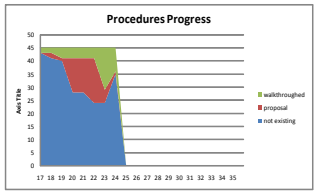
ISO 13485 project improvement approach

- Implementation = normal project
  - Assign a project leader
  - Make a project plan
  - Define deliverables
  - Plan and track
  - Report back to management on regular basis
  - Assign process owners
  - Pilot new procedures
  - Deploy the new QMS
    - Train people
    - Easy access to QMS
    - Check via audits



ISO 13485 project Way of Working & Global Plan

Tracking



Walkthroughs of flow charts and proc interfaces at weekly progress meeting leading to informal updates

QMS publication board For pilot project(s)

Publish After walkthrough

Electronic Reviews (no meetings): should only reveal minor issues.

Publish After E-reviews Or annex written

QMS publication board For pilot project(s)

- ☐ Training Done
- ☐ Management Review done
- ☐ Process audits done

- ☐ Stage 1 Certification
- ☐ QMS approved

- ☐ Stage 2 Certification

☑ **Start Project**

01-2010

Define
- Q Manual
- Q Index
- Pilot project(s) @hmic

04-2010 Week 18

- ☑ Q Manual / Index walkthroughed
- ☐ Pilot projects defined

Walkthroughs

Process Owners:
Write (buddy with WBig)
- Parts of Procedure Interfaces
- Flow charts

WBig
- Total procedure interfaces
- Design webinterface

08-2010 Week 35

☐ **All red and orange procedures synchronised with each other (proposal)**

Official e-reviews Q Manual & procedures

- Write annexes, check with 1 peer and publish
- Xtra text flowcharts (front, back)

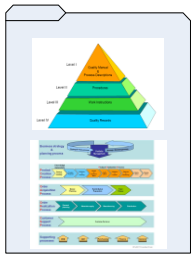
10-2010 Week 43

Write / Executing Training. At least: Quality Policy

12-2010 Week 52

Gather evidence In pilot Project(s)

Quality Manual
- Quality Policy
- Organisation
- Scope
- Processes
- Process descriptions
- Process Onwers



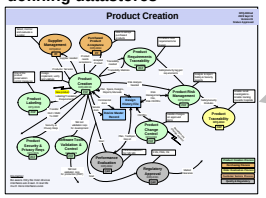
Annexes
- default English
- in Dutch if users are Dutch speakers only

Templates

Guidelines

Work instructions

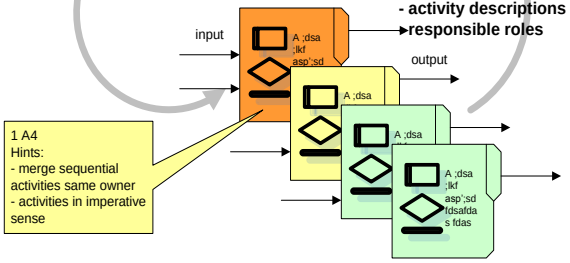
Procedure interfaces
- connecting flow charts input/outputs
- defining datastores



Update of A&D file by all owners

Abbreviation & Definitions file

Flow charts *(incl. blue italic)*
- scope
- input / output / datastores
- activity descriptions
- responsible roles



1 A4
Hints:
- merge sequential activities same owner
- activities in imperative sense

Quality Manual Index File
- procedures per process
- process owner

Procedure A process A
--- Template A
--- Work instruction A
--- Guideline A
Procedure B process B
-- Template B
-- Template C
Procedure C process A
Procedure D process C
-- Guideline B

Priorities:
Red = High (ISO, needed for project))
Orange = Medium (ISO)
Green = Low (non ISO, CCM wish)

Discussion