Quality Assurance

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Disclosure for Lilli Møller Andersen

No relevant financial relationships exist for any issue mentioned in this presentation

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Agenda

- Quality Assurance
- Quality Management System
- Quality Risk Management
- Validation Master Plan
- Introduction to group work

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Quality Assurance

- *Quality Assurance is a wide-ranging concept, which covers all matters, which individually or collectively influence the quality of a product*
- *It is the sum total of the organised arrangements made with the objective of ensuring that medical products are of the **quality** required for their intended use*

Ref : Eudralex part 1

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Quality

- *The quality of something can be determined by comparing a set of inherent characteristics with a set of requirements**
- Characteristics include

  Product quality (safety and efficacy)

  Compliance with regulatory requirements

  Allowing deliveries with acceptable costs of production

**Ref : ISO 9000*

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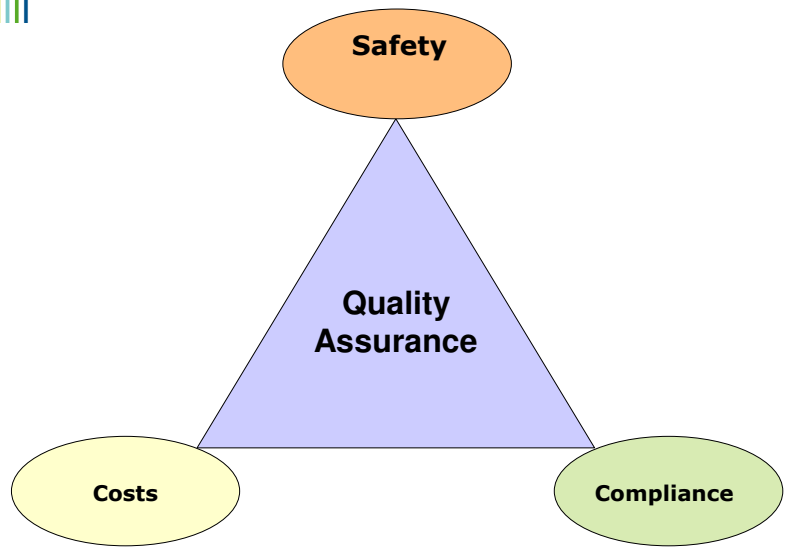
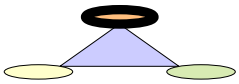


Safety



- Activities relates to prevention of adverse events and other drug related problems
- Efforts ultimately links to the protection of the patient
- On-going attention to the risk-benefit balance specific for the product
  - Pharmocovigilence based on Risk Management
  - Scientific knowledge and relevant experience required
  - Any safety concern to be evaluated
  - Detailed requirements for interactions with the authorities

Monitoring Safety in a hospital pharmacy

Pharmacovigilance

- Investigations in relation to reported Adverse Effects (AE)
- Survey of relevant literature
- Data from clinical studies

Handling of technical complaints

- Complaints not reported as adverse effects

Surveillance of trends

- Trend-reporting of complaints and AE's
- Trend reporting of deviations
- Stability studies
- PQR

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Compliance

Meeting the requirements of the current GMP as they relate to *your* products

- Include conformance to official requirements as
  - Laws
  - Guidelines and standards
  - Pharmacopoeias
  - Regulatory files (MA, SMF)
- Interpretations are done by the health authorities
  - In general no differences between the pharmaceutical industry and hospital pharmacies
  - In reality compliance is a moving target based on evaluation of risks and on-going negotiations regarding "good enough"
    - Take benefit of your position

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Compliance in a Hospital Pharmacy

- Rooted in the Quality Management System
- Adjustments as required
  - For-cause dialogue with authorities
  - Inspections
    - Completed by national authorities
    - Scheduled or for-cause
    - Approaching requirements to the industry
    - Increasing harmonization within Europe and world wide
  - Internal audits
    - Directive 2003/94/EC
    - To be conducted on a regular basis
    - To be documented

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Costs

Effectiveness in production and continuous improvements in production and deliveries are also quality goals !

- In general increased product quality with decreased number of irregularities
- More patient value for the same money

Quality work is also repeatedly arguing for "doing the right the first time"

- Early quality related efforts are important
  - Cost/benefit analysis in Business Plans
  - Investments may also include costs related to training and validation

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Quality Management System

- *To achieve the quality objective in a reliable manner there must be a comprehensively designed and correctly implemented **system of Quality Assurance** incorporating Good Manufacturing Practice and thus Quality Control. It should be fully documented and its effectiveness monitored*
- *The establishment and maintenance of a satisfactory **system of Quality Assurance** and the correct manufacture of medicinal products relies upon people*

Ref : Eudralex part 1

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People

Continuous training must be documented

- Appropriate to the duties assigned
- Include GMP and Hygiene programmes
- Specific training if hazardous materials
- Include all groups of personnel
  - Also technical staff, cleaning workers etc.

The person responsible for release of products must be different from the person responsible for production

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System of Quality Assurance = Quality Management System (QMS)

- Incorporate the principles of
  - GMP
  - Quality Control
  - Quality Risk Management
  - Internal requirements and aspirations

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QMS /1 GMP

Requirements include (among other things):

- Approved SOPs
- Validation of critical attributes
- Change Control
- Traceability of activities and materials
- Records providing the full history of each batch
- Any deviation investigated and documented

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QMS/2 Quality Control

- Include (among other things):
  - –Sampling, inspection and testing
    - GMP materials as well as finished products
  - –Validated test methods
  - –Environmental monitoring
  - –Reviewing of documentation for manufacturing processes
  - –Release by a Qualified Person

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QMS/3 Quality Risk Management

- An integral part of most QA related activities

- Key elements
  - High lights potential harms to the patient
  - Utilizing product and process understanding
  - Insist on data
  - Document considerations and decisions
  - Prioritize efforts

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Quality Risk Management

- Extensive applications. Ex. :
  - –Development of products and processes
  - –Environmental monitoring
  - –Change Control
  - –Deviations (release or not release)
  - –Validation
    - VMP, Protocols

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The Validation Master Plan (VMP)

- *The key elements of a validation programme should be clearly defined and documented in a VMP*
- *The VMP should be a summary document which is brief, concise and clear*
- *In large projects it may be necessary to create separate VMP's*

Ref. Eudralex annex 15

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- The VMP should contain data on at least the following
  - Validation Policy
  - *Summary of facilities, systems, equipment and processes to be validated
  - *Organisational structure of validation activities
  - Documentation format: the format to be used for protocols and reports
  - Planning and scheduling
  - Change control
  - Reference to existing documents

Ref. Eudralex annex 15

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Introduction to Group Work

"Design a VMP based on risk evaluation"

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Quality Risk Management

*"No one tool or set of tools is applicable to every situation in which a quality risk management procedure is used" **

**Ref: Eudralex Annex 20*

Risk = S x O x D

S = **S**everity of harm
O = Probability of **O**ccurrence
D = Likelihood of **D**etection

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	Low	Medium	High
Severity	Will for sure not cause harms 1	Unlikely to cause harms 3	May cause harms 5
Occurrence	A rare unusual event 1	Occur from time to time 3	Common/well known event 5
Detection	Very high likelihood of detection 1	May be detected 3	Will not be detected 5

Risk=SxOxD

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Risk identification

- Critical quality attributes in relation to the product
  - Purity - chemical and microbiological
  - Homogeneity
- Quality of materials
  - API, excipients, packaging materials, materials in contact
- Facilities, equipments and systems
  - Classification ?
  - Risk of contamination or cross-contamination
  - Dedicated ?
  - Open or closed ?
- Processes
  - Manual or automatic
  - Imprints ?
- Controls
  - In process controls
  - Test methods
- People
  - Education and training
  - SOPs

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Risk evaluation

- Calculate the risk-score for each critical parameter
- Rank the risk-scores
- Prioritize activities taking risk-scores into consideration
- Out put from the Quality Risk Management Process to be used for e.g. the Validation Master Plan

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The tasks:

- Prepare a summary of facilities, equipment and processes to be validated
  - Broad description of products and facilities
    - E.g. dosage forms, locations, processes, major equipment, utilities and sterilisation methods
  - Conclusions from Quality Risk Assessment
- Describe the structure of validation activities
  - Grouping of validation activities
    - E.g. equipment, facilities, HVAC, cleaning, CRS, personnel (media fills)
    - Structure of documents (Validations Plans, protocols, reports)
  - Planned sequence of activities

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Supporting slides

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Definitions and Abbreviations

1. CRS

   Computer Related System

2. Harm

   Damage to health, including the damage that can occur from loss of product quality or availability

3. HVAC

   Heat, Ventilation and Air Conditioning

4. SOP

   Standard Operation Procedure. I.e. procedures, instructions, manufacturing formulae and specifications

5. VP

   Validation Plan. Collect a inter-related group of protocols

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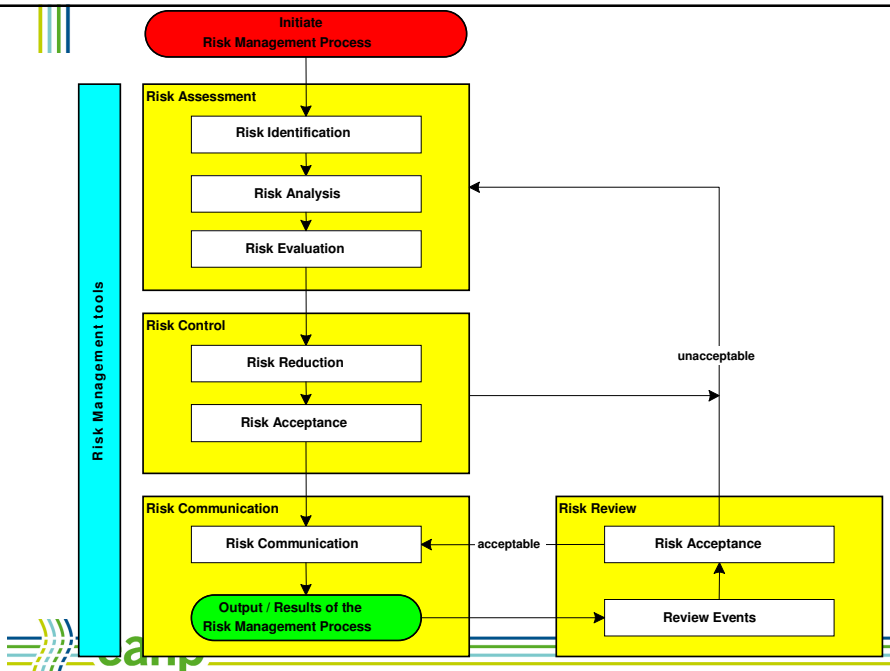

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