Good Manufacturing Practise

- ## Quality Management

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- Uppsala Universitet Spring term 2007

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Quality Management

- **Quality assurance**
  - total arrangements to ensure that products are of the quality rquired
- **Good Manufacturing Practise**
- **Quality control**
  - Part of management which ensure relevant test of product before release

Radiopharmaceuticals

- Characteristics
  - Parenteral administration
  - Radioprotection mandatory
  - Short physical half-life
    - Ex-temporous preparation, low volume
    - Few patients given each batch
    - ”Parametric release”
  - Low concentrations
    - Low toxicity

Quality assurance

- What ?
- Why ?
- Who ?
- When ?
- Where ?
- (How ?)

Quality Assurance

- Quality Management
- Yesterday
- Good Manufacturing Practise
- Today
- Quality control
- Tomorrow before release

Development of QA

- Risk assessment
- Environmental
- Occupational
- Company — Total quality — Identification
- Process — Quality management — Conviction
- Product — Quality assessment — Insight
- Quality control — Constraint

- 1960 1970 1980 1990 2000

Quality Management

- In the planning of the site (Sic !!!)
- Based on site objectives and production
- Based on Quality aims
- Documented in Site Master File

Quality management

- Responsibility:
  - Manager
  - Medical responsibility
  - Pharmaceutical responsibility
  - Safety (e.g. Radiation safety, IT..)
  - Computer responsibility
  - Quality officer

Qualified person, QP

- ”A designated position for a suitable trained person fully responsible for certification of products”

Quality organisation

- Special unit for quality assurance
- Authority to approve and reject
  - preparations, materials, labelling etc
  - specifications and procedures, methods
  - implement revalidation
- Authority to review production
- Authority confirmed in writing

Quality aims at Uppsala Imanet

- Correct, verified and quality controlled in sufficient yield
  - Identity (radionuclide and product)
  - radiochemical and chemical purity
  - given specific radioactivity
  - sterile and free from endotoxins
- in adequate time
- with adequate radiation protection
- with adequate information to personell
- based on risk analysis

Good Manufacturing Practise

- Purpose
  - medicines are made, stored and distributed so that they are safe and effective
  - Directives 75/319/EEC
  - ..
  - 91/356/EEC
  -

Good Manufacturing Practise

- Achieved by..
- ….organised activities, properly designed and monitored facilities, controlled procedures, full and proper records and full traceability

Good Manufacturing Practise

- Approved and validated procedures are described in:
  - Standard Operating Procedures, SOP
  - Radiotracer monograph, SPC
  - Batch protocol (synthesis protocol)
  - Delivery protocol (for release)

Good Manufacturing Practise

- Facilities
  - adequate for handling of materials and equipment
  - prevention of contamination and mix-up by personell, substances or environment
  - same room can be used in PET for several purposes (e.g. synthesises)

Good Manufacturing Practise

- Aseptic work
  - adequately controlled to limit presence of microorganisms
  - critical activities in Class A (Class 100) e.g LAF or isolator
  - Class 100 in Class C in turn in Class D
  - critical activities e.g. assemply of sterile material for/and sterile filtration

Good Manufacturing Practise

- **Aseptic work area**
  - cleaned daily
  - people present at a minimum
  - minimum of material in LAF
  - designated coats, arm protection, glove
  - sanitation of material before entry
  - equipment qualified, documented
  - cleaning and maintenance validated

Good Manufacturing Practise

- Production and process controls
  - Consistent production and processes
  - Written documents (Master, batch record)
  - Batch record form adequately filled out
  - Batch retained 1 year for new QC
  - Inspection of cleaning
  - Micobiological control of aseptic work
  - Validation and qualified by QA

Process control- Quality control

- Quality should be built in the process

Quality control

- The quality control is concerned with
  - Organisation
  - Specifications
  - Test procedures
- for the release of product
  - ensuring that relevant control tests are carried out against approved and validated procedures

Quality Control

- Radionuclide identity
- Radionuclide purity
- Radiochemical identity - all batches
- Radiochemical purity - all batches
- Sterile for parenteral use
- Free of endotoxins
- pH
- Residual solvents, etc

Parametric release

- Release of product before all quality controls of the batch have been finalised and validated

- Requires proper pre-test quality controls and validation

Quality Control

- Chemical identity and purity must be proved with at least two independent analytical chemical methods (e.g. Chromatography and NMR).
- Two independent analytical chromatographic procedures must be employed

Quality Control/Assurance

- Acceptance criteria met by each batch
- Sterility test not performed before release
- Acceptance criteria are documented
- Before, shiping container must be labelled
- QC includes stability test made for 3-5 batches
- Written procedures for withdrawal and complaints. SIC !! The role of QA

Quality control

- Quality markers at Uppsala Imanet
  - radiosynthesis released/failed
  - delivery on scheduled time +/-10 min
  - aseptic test of products and staff performance
  - airborne particles in production area
  - downfall of microbes in hotcells/labs
  - cyclotron or Synthia ”up-time”

- **Withdrawals and complaints**

- **Written procedures for withdrawal and complaints.**

- **SIC !! The role of QA**

Contract Manufacture and Analysis

- Approved contract between site and external supporter
- Description of GMP in the contract
- Assessment of GMP compliance of the supporter

SELF INSPECTION

- Activities during self inspection must comply with quality aims
- Effective and efficient
- Document the self-inspection system and the follow-up actions
- Results must be brought to attention by personell responsible for the activity
- Responsible persons must take timingly corrective actions

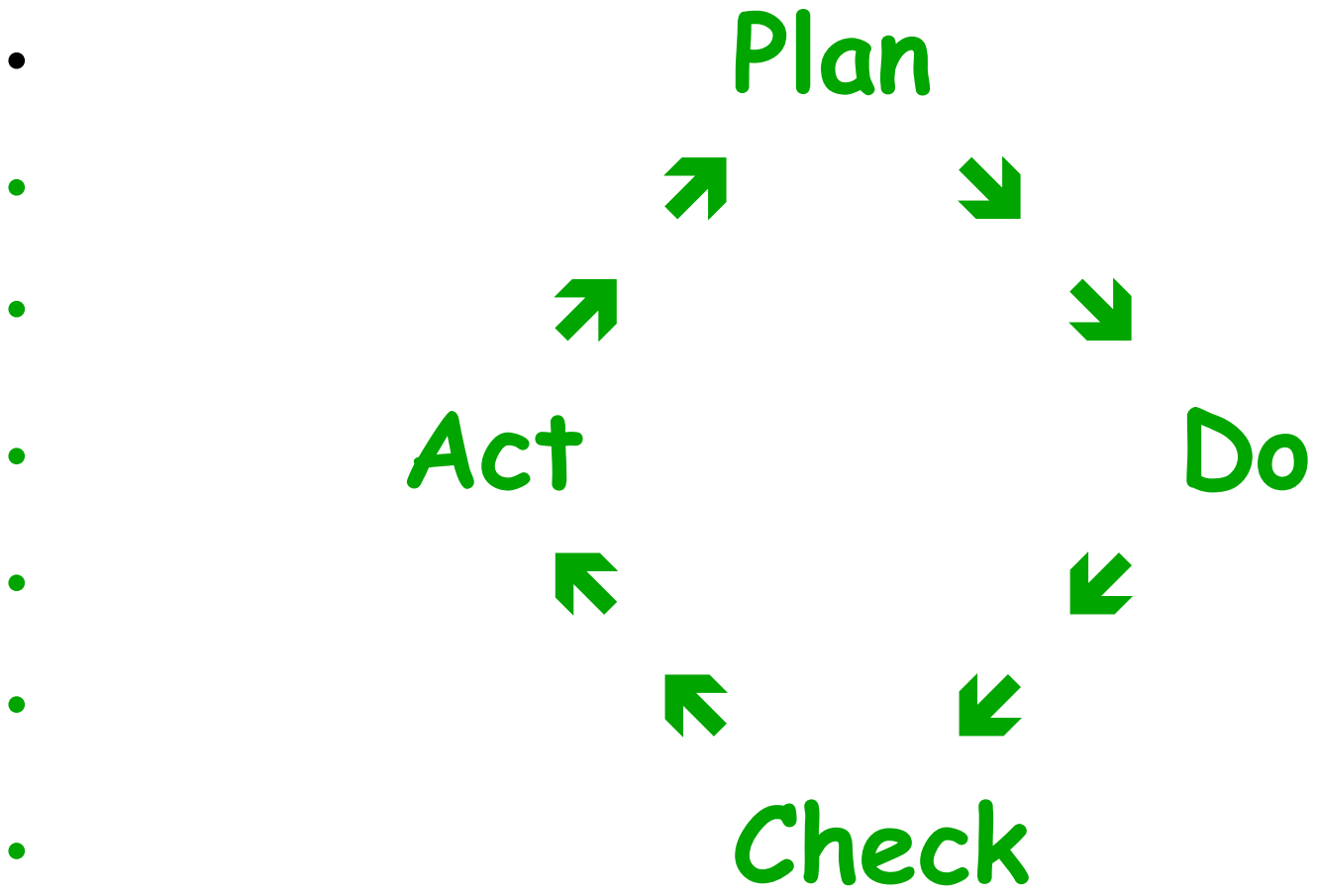
Quality Management

- Quality measures for success:
  - High quality starting material
  - Good design of premises and equipment
  - Validated process
  - In process controls and not least
  - Well-educated, well-trained and motivated personell

Good Manufacturing Practise

- *Pelle advices*
  - Common sense - ambition
  - Build system from aims and objectives
  - Parametric release
  - Quality part of the process, involve staff
  - QA is for patients and personell (not for authorities)

The quality circle



Quality Assurance

- It is a long sailing tour !!!