

# Quality aspects during Prequalification Evaluation of vaccines

DCVMN meeting  
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# Outline

- Differences between vaccines and pharmaceutical
- Quality relationship
- GMP concept
- Quality aspects during PQ evaluation
- Regulatory consideration
- Programmatic considerations
- Site audit

# Pharmaceuticals Vs Vaccines

## Pharmaceuticals

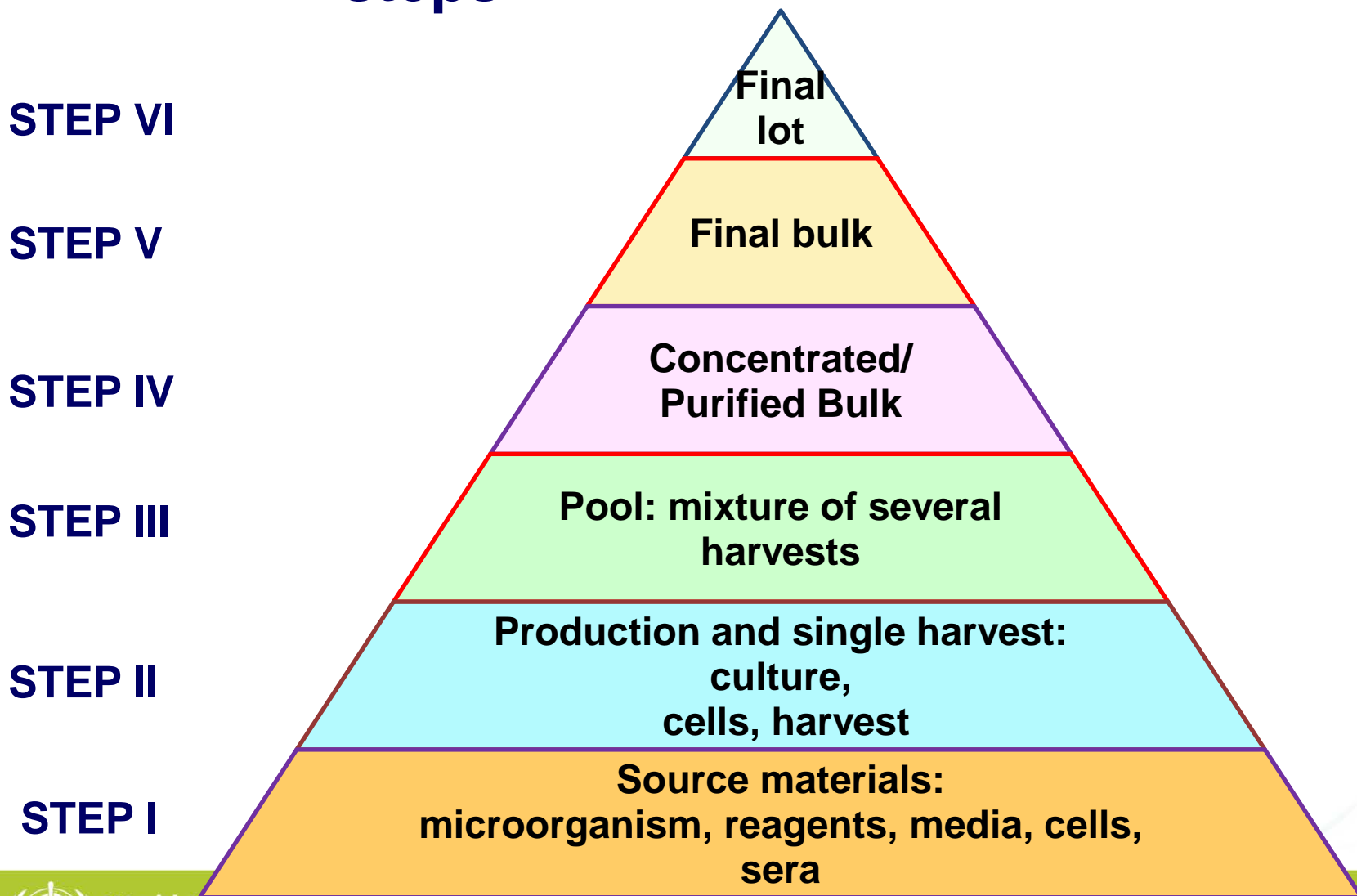
Produced and controlled using physicochemical methodologies

## Vaccines

### Quality considerations

- Raw materials
- Manufacturing processes
- Quality control methodologies

# Generic vaccine production steps



# Each vaccine is an unique product

**Different strains of bacteria or viruses can be used by different manufacturers for the same vaccine**

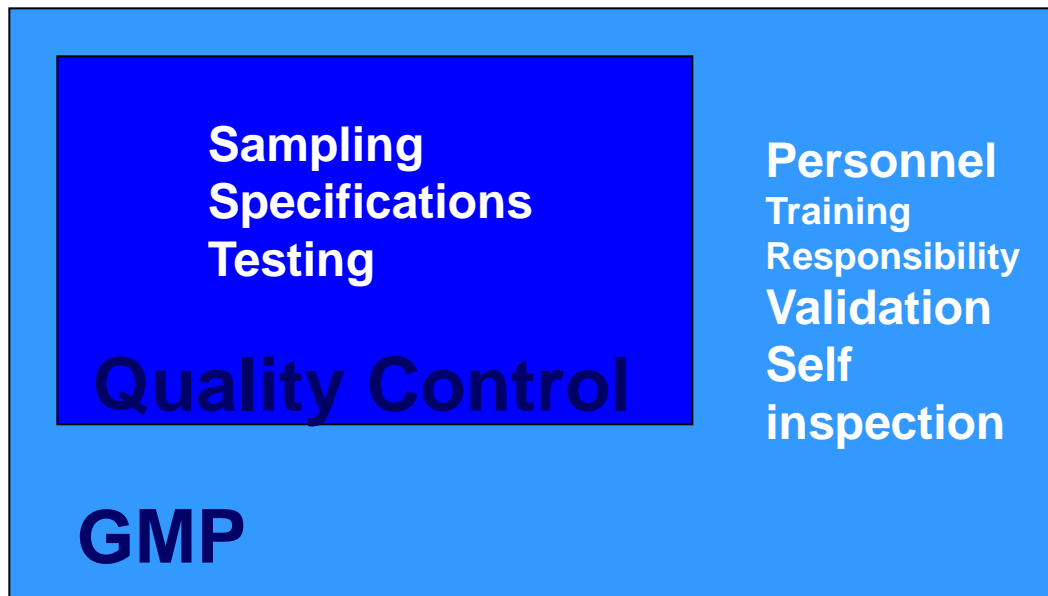
» (eg Measles: Schwartz or Edmonston Zagreb)

**One company may make their vaccine in many bottles, and another may make the same vaccine in a single large fermentation tank.**

**The same virus may be grown in one type of cell by company A and in a different cell by Company B.**

**The same vaccine from one company may not use the same stabilizers or preservatives as another company.**

# Quality Relationships

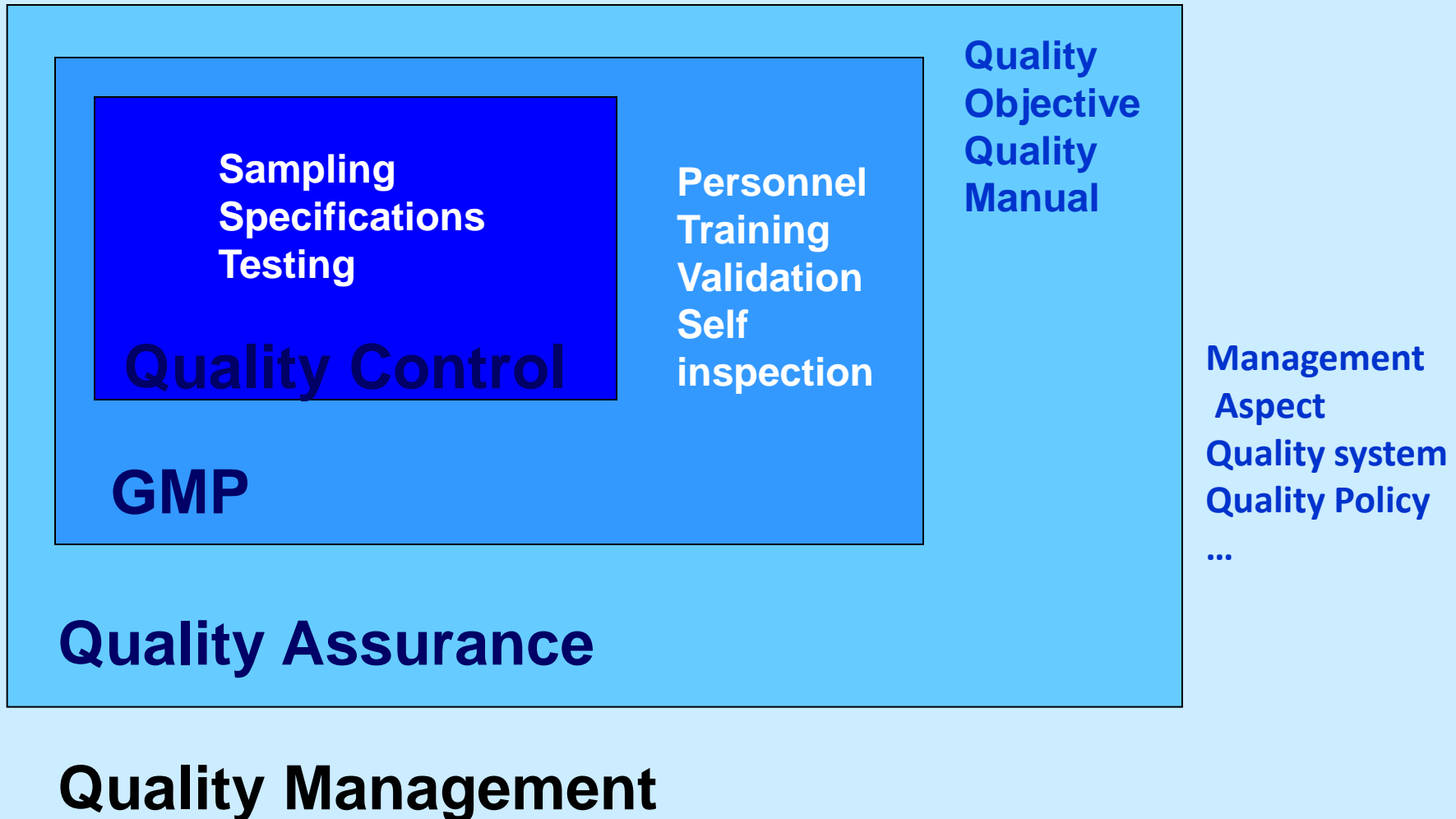


# Good Manufacturing Practice (GMP)

World Health Organization defines GMP as:

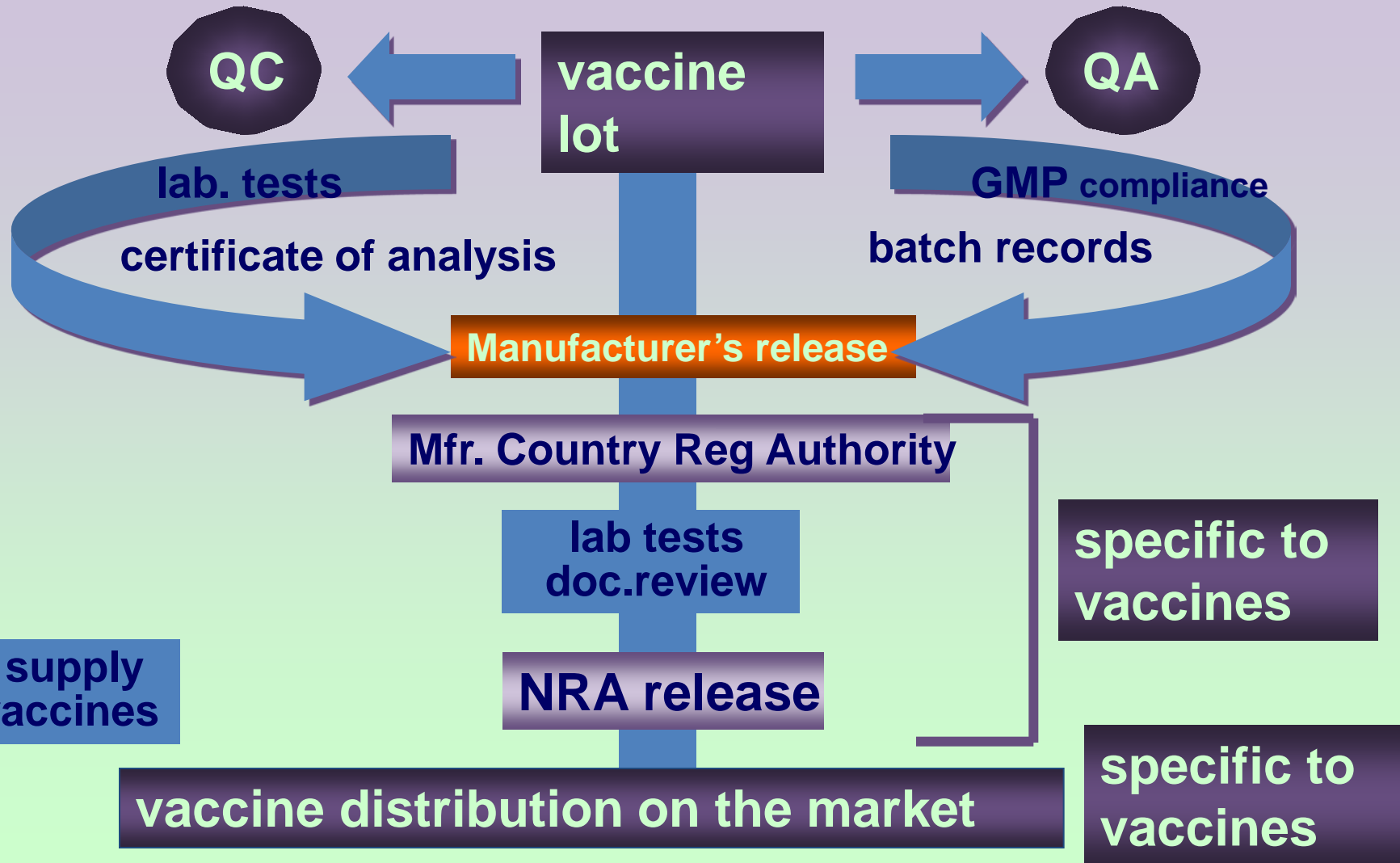
”that part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization”

# Quality Relationships





# Complex release process



# Quality aspects during PQ evaluation

# Specific aspects considered

- General understanding of production process and quality control methods
- Production consistency at commercial scale (assessed by testing of samples of final product)
- Compliance with GMP
- Compliance with WHO recommendations and UN tender specifications including labels and inserts
- Programmatically suitable presentation
- Clinical data relevant for the target population in the recommended schedules

# Chapter 5: Production

- ✓ **5.1 Manufacturing formula**
- ✓ **5.2 Description and flow chart of Manufacturing & testing**
- ✓ **5.3 General policy for process validation**
- ✓ **5.4 Handling starting material, packaging material, bulk and finished products (Sampling, quarantine, release and storage).**
- ✓ **5.5 Handling and procedures for destruction of rejected materials and products.**

# Chapter 6: Quality Control (1)

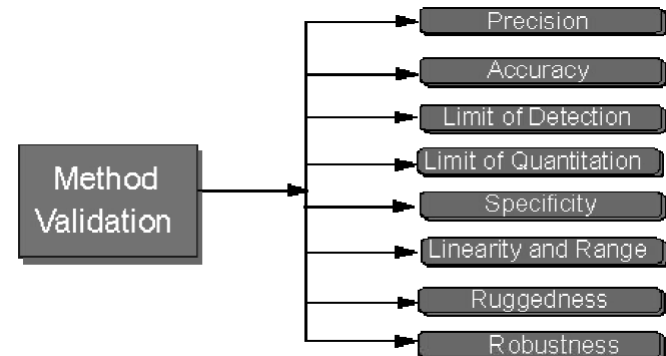
- ✓ **6.1 Starting material**
  - ✓ **6.1.1 Raw material**
  - ✓ **6.1.2 Labelling and packaging**
  - ✓ **6.1.3 Qualification of suppliers**

# Chapter 6: Quality Control (2)

- ✓ 6.2 Intermediate products
- ✓ 6.3 Finished product

## Specifications and routine tests

## Validations



# Chapter 7: Stability data

## 7.1 Intermediate products

## 7.2 Finished product : vaccine

## 7.3 Finished product : diluent & reconstituted product

## 7.4 Policy for assigning the date of manufacture of each component, final product and diluent

# Regulatory considerations

- Need to ensure that adequate regulatory pathway is in place, that product is licensed, continuous regulatory oversight in place
- Need to assess quality
  - Adequacy of production process
  - Adequacy of quality control methods and specifications
  - Stability data
  - Transferability of testing methods to NCL and independent labs
  - Consistency of production
  - GMP compliance, adequate Quality Management System in place



# Programmatic considerations (1)

- Vaccine used in the country of origin?
- Compatible with the existing EPI schedules?
- Stability profile: understanding of the cold chain requirements/ suitability for use under field conditions
- Stability profile: VVM category required
- Packaging: Volume of cold space required

# Programmatic considerations (2)

- Presentation/primary packaging suitable?
- Open vial policy applicable?
- Information on inserts: adequate?, clear, reflects product characteristics? Available in all required languages?
- Transport boxes validated for international shipments?

# Outcome of the review of PSF

**Scenario 1:** PSF review does not raise any outstanding issues

**Scenario 2:** PSF review raises outstanding issues for clarification/additional information (no major)

**Scenario 3:** PSF review raises major technical and programmatic issues

**Consistency testing is scheduled**

**Outstanding issues may be followed up at site audit &/or request for additional information**

**Consistency testing is scheduled**

**Ad Hoc committee is convened**  
Request for additional information to give final recommendation  
Stopping the PQ

## Timing for site audit

File review  
quality and  
clinical  
completed

Consistency  
Testing  
completed

Satisfactory outcome

**SITE AUDIT SCHEDULED**

# Objectives



Product is produced in accordance to WHO GMP recommended requirements



Product meets the WHO recommended requirements for quality, safety and efficacy (TRS documents)



Product meets the specifications of the UN tenders

# Scope of Site Audit

- **Personnel- Organization**
- **Facilities and Equipment (Warehouses, production areas, QC laboratories, animal house, etc)**
- **Utilities**
- **Quality systems, Quality Assurance unit**
- **Production process and in process controls**
- **Quality control facilities, equipment and methods**

# Aspects considered: Quality System

**Quality assurance unit, roles and responsibilities**

**Documentation system, documentation and records control**

**Training program**

**Post-marketing surveillance, including investigation of complaints  
and safety and efficacy reports**

**Vendors qualifications**

**Lot release system**

**Investigation of complaints**

**Validation master plan**



## Aspects considered: Quality System

**Handling and investigation of deviations**

**CAPA,**

**Recall, returns and destruction procedures**

**Reprocess, Rework and Returned Product**

**Internal and external audits**

**Personnel**

**Annual Product Review**

**Maintenance Program, pest control, environmental control**

**Site master plan**

**Note: List is not comprehensive**





# Production System

**Media preparation area and process**

**Bulk production area and process**

**Storage areas**

**In process controls**

**Change over procedures**

**Environmental monitoring**

**Gowning procedures**

**Formulation and filling**



Courtesy of IDT Biologika

# Production System

**Inspection**

**Labeling, Packaging and Shipping procedures**

**Change over procedures**

**Change Control**

**Handling of Deviations**

**Procedures, Process and systems validation**

**Sanitation and hygiene: Cleaning validation**

**Batch manufacturing records**

**Note: List is not comprehensive**



# Quality Control System

**Testing methods in place and their validation**

**Tests for intermediates and final products**

**SOPs**

**Sampling procedures**

**Stability Program**

**Documentation control**

**Quality control facilities and equipment, including animal house**

**Test results and trends- Handling of out of specifications**



**Note: List is not comprehensive**

# Facilities and Equipment

**Quality of construction, flow of: personnel, product, materials, wastage and process**

**Utilities (HVAC, Pressure differentials, water systems, clean steam, compressed air)**

**Clean rooms, Classification**

**Equipment qualification: DQ, IQ, OQ and PQ**

**Equipment calibration and verification**

**Validation of computerized systems**

**Note: List is not comprehensive**

# Key elements for success

**High commitment from management to Quality Products and to implementation of Quality Systems**

**Full independence between production, Quality Control and Quality Assurance.**

**Sound and controlled documentation system, detailed procedures (SOPs), detailed records (BPR)**

**Well trained staff recording all data in BPR immediately, second check by supervisor. Staff trained to opening deviation reports and related investigation**

**Presence of QA in production, major role in review of records, investigation of deviations, internal audits and CAPA system**

**QC and QA dimensioned and equipped to match production capacity in volume and diversity of products**

## **Main reasons for failure**

**Lack of commitment from management to Quality**

**Roles and responsibilities at different levels not well defined**

**Wish to rush products into the market without enough process robustness and experience**

**Weak QA, weak quality systems in place not matching production needs**

**Show driven by production head or directors**

**Lack of transparency and honesty with auditors**

**Lack of capacity to identify, investigate and correct gaps in their systems**

# Site Audit Outcome

