Revision of WHO GMP for biological products
-Briefing DCVMN meeting

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First WHO GMP for pharmaceuticals was published in 1968


Current version of WHO GMP for pharmaceutical products: main principles (TRS 986)

WHO GMP for biological products (TRS 822)

WHO good manufacturing practices for sterile pharmaceutical products, 2011

WHO good manufacturing practices for blood establishments, 2011
Request for revision

- Widely used or adopted by regulators
- Mandatory guidelines for medicine and vaccine prequalification programmes

- Strong request for revision and updating of GMP for biologicals

- First attempted revision initiated in 2007
  - Working group meeting in 2007
  - Preliminary draft in 2008
Revision process

- Second attempt:
  - Drafting group meeting in Oct 2013

- Consultation July 2014
  - Participants (42): NRAs, industry, GMP experts
  - Reviewed the first draft and agreed on the principles
  - 3rd draft has been prepared by drafting group in light to the comments of the consultation

- Public consultation on WHO website

- Drafting group meeting in April
Challenges during the drafting process:

- Definition of Biologicals
- Supplementary Document (Fill-in the Gaps to existing document: 961,986 etc.)
- To give ORIENTATION on Strategy and Focus of requirements for Biologicals without indicating the “How-to-do”
- To consider vaccines and other biologicals equally
Revision principles

- Annex to the GMP: Main principles for pharmaceuticals
- Principles in Sterile pharmaceuticals to be applicable
- Focus on special consideration to biologicals
  - e.g. QMS, QC, Quality Risk Assessment, Biosafety, Environment monitoring, Production, Campaign production, Classified area, Animal quality, Starting materials, etc.
- Other related publications to be referenced
  - Process Validation for Biologicals.
  - Environmental Monitoring for Biologicals
  - Risk Assessment (based on ICH Q9 and TRS 981 Annex 1).
# Content of draft revision

- Introduction
- Scope
- Glossary
- Principles and general considerations (including PQS and QRM)
- Personnel
- Starting and raw materials
- Seed lot and cell bank
- Premises and equipment
- Containment
- Clean rooms
- Production
- Campaign production
- Labelling
- Validation
- Quality control
- Documentation (lot process records)
- Use of animals
**Key changes/updates/recommendations**

- **Scope:**
  - Apply to commercial manufacture and testing
  - To manufacturing procedures

- **General considerations:**
  - Annex to GMP main principles
  - Biological nature: variability, sensitive, contamination
  - Aseptic risk
  - Emphasize in-process control
  - Consistency
  - Importance of QRM
Key changes/updates/recommendations

● Starting materials
  – Seed lot and cell bank system
  – Free of adventitious agents
  – Condition of transportation

● Personnel:
  – Scientific requirement, especial qualification of key personnel
  – Requirements for BCG and blood derivatives production
  – Vaccination
  – Special training
  – Cross contamination control
Key changes/updates/recommendations

- Premises and equipment
  - Live organisms and spores are prevented from entering non-related areas or equipment
  - Control measures to remove the organisms and spores before the subsequent manufacture of other products by means of HVAC and validated cleaning and decontamination procedures
  - Environmental monitoring specific for the micro-organism being manufactured
  - Use of separate animals for production of vaccines and testing in the QC
  - No animals should be used in production area for in process or final testing purpose.
Key changes/updates/recommendations

- Campaign-based manufacturing facility layout and design of the premises and equipment shall permit effective decontamination by fumigation
- Killed vaccines, including those made by rDNA techniques, toxoids and bacterial extracts may after inactivation be dispensed into containers on the same premises as other similar sterile biological products
- Storage of Seed lots and cell banks storage in separate area with restricted access
- Dedicated production areas (Upstream Processing Area) where live microorganisms are handled. Only up to Pre-purification (removal of cell debris) activities shall be handled in this area
- Spore forming organisms in dedicated facility
Key changes/recommendations

– For bulk and fill finish, risk based approach and with proper justification for each product to be handled. Important to have bracketing principle

– Validation of campaign change procedures and proper acceptance criteria for traces based on available toxicity data or traces producing affect on untoward mix-up or cross contamination

– Use of additional analytical technique with higher sensitivity for checking traces/residue for campaign production as compared to normal production
**Issue to be followed and next steps**

- Companion document to be developed
  - Validation (process and assay methods)
  - Campaign production
  - Quality risk assessment
  - Biosafety assessment

- Definition of biological medical products

- Ensure the input of biotech industry at the next consultation

- Leading time of implementation of the revised GMP

- Next round public consultation (July-sept 2015)

- Review by ECBS 2015 October
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- Participants of Consultation in July 2014 and commenters during first round public consultation.

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