Compliance with the GMP Standard in the International Level

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Outline

- Provisions under the Drugs and Cosmetics Act, 1940
- GMP Standards
- Various GMP requirements
- Inspection procedure
- GMP - Common deficiencies
- Regulatory Actions

Drugs and Cosmetics Rules, 1945

- License is required for manufacture of drugs, both for domestic and export purposes
- License is issued subject to conditions
- Licensed manufacturer is required to comply to GMP prescribed under Schedule M.
- There is no exemption for facilities manufacturing drugs for export.
- In addition to the requirements under Schedule M, the exporting facilities have to comply to the requirements of the importing country

Provisions under the Act: Inspectors

- appointed under the provisions of the Act either by Central or State Governments
- operate within their jurisdiction specified subject to instructions
- Authorised to inspect manufacturing/sale/clinical trials sites
- Notified for specific products such as drugs and cosmetics or Medical device
- subject expert is coopted in certain specialised products

GMP Standards

GMP Standards

- Schedule M of Drugs and Cosmetics Act and Rules and QMS for Medical Devices
- WHO TRS guideline for exports
- As per EU directive for export of API's

Tools of Inspection:

- Rules
- Checklists
- SOPs and
- CDSCO guidance document for zonal office

Compliance with the GMP

- The GMP requirements vary from country to country. They can be broadly classified as under:

  - GMP of the exporting country.
  - WHO CPP
  - GMP of the importing country
  - GMP as required by the procurement agencies.

Schedule M: GMP

- Countries which do not have well defined regulatory requirements generally accept the GMP of the exporting country.

- The compliance to GMP is verified by the State Drugs Inspector during the annual inspection.

- A joint inspection by the state and central inspectors is carried out once in every three years to verify GMP compliance.

Frequency of Inspections

- Inspector is required to inspect the manufacturing facilities under his jurisdiction once a year
- Inspection by a joint team of Central and State inspectors once in three years
- Inspection by the joint team upon application for CPP or EU WC

WHO CPP

- WHO CPP is voluntary.
- CPP inspection is carried out by a joint inspection team comprising of the State and Central Inspectors.
- It is product specific.
- Validity is limited to 3 years.
- Facility is re-inspected at the end of 3 years for re-certification.
- Compliance to WHO GMP is in addition to Schedule-M GMP requirements.

GMP of importing country

- The compliance to the GMP of the importing country is verified either by the Indian NRA or by the NRA of the importing country.
- CDSCO has been carrying out inspections for verifying the compliance to GMP as specified in the EU Directives for export of APIs.
- In other cases the importing country has been inspecting the Indian manufacturing facilities.
- In such cases the observations are not communicated to the Indian NRA.
- Though the facility may be complying to the requirements of Schedule M may not meet the requirements of the importing country.

Inspection Procedure

- Application
- Assessment
  - Completeness of application
  - Technical Review (Site Master File, DMF, complaints, changes in facility, technical staff etc.)
  - Planning for inspection
- Notification of inspection date to firm
- Inspection duration – 3 to 5 days

Inspection Procedure

- Inspection 3-5 days focusing all critical areas
  - Opening Meeting
  - Documentation – Change Control, CAPA, Validation, OOS / OOT, deviations control, Product/process characterization, annual product quality review, consistency, SOPs, training, etc.
  - processing
  - Personnel
  - System
  - Facility
  - Including service and ancillary areas
  - Exit meeting
- Inspection Report
- Review
- Letter for Compliance
- Review of compliance
- Final action

SOP No. INS –QA-002 GMP inspection and report writing

SOP No. INS –QA-007 Procedure for Planning and Preparation of Gmp Inspection

GMP - Common deficiencies

- Lack of proper written procedures
- Where written procedures are available they are not followed
- failure to thoroughly review any unexplained discrepancy/deviations
- Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established, written, or followed
- Inadequate Change control procedures
- Improper handling of out-of-specification(OOS)

GMP - Common deficiencies

- Complaint investigation
- Corrective action of deviations
- Product quality review,
- Failure to evaluate the potential impact of changes on quality of the product
- Batch manufacturing record –not comprehensive
- Improper selection of supply chain and material control without risk assessment.
- Poor understanding of quality risk management principle

Regulatory Actions

- Regulatory actions are being taken against manufacturers for non compliances as per the provisions under the Drug and Cosmetics Rules
- Regulatory actions include
  - Warning Letters
  - Suspension
  - Cancellation
  - Prosecution

Thank You !