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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Finished Product Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	Cipla Ltd
Corporate address of manufacturer	Cipla House Peninsula Business Park Ganpatrao Kadam Marg Lower Parel, Mumbai-400 013 India
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Cipla Ltd Plot No L-139, S-103 & M-62, Verna Industrial Estate, Verna Salcette, Goa, 403 722, India
Unit/block/ workshop number	Unit III, Unit IV, Unit VII, Unit VII PDII, Unit VIII
Inspection details	
Dates of inspection	18-20 and 22-23 March 2019
Type of inspection	Routine inspection
Introduction	
Brief description of the manufacturing activities	CIPLA Ltd Goa has ten manufacturing units. More specifically: 1. Unit I manufactures Nasal Spray, Ophthalmic and Optic Drops, Respiratory Solutions and Suspensions (Unit dose / Multiple dose), 2. Unit II manufactures Pressurized Metered Dose Inhalers, 3. Unit III manufactures Tablets, Topical Preparations, 4. Unit IV manufactures Tablets, Hard Gelatin Capsules, 5. Unit V manufactures Cytotoxic Injectables: Liquid and Lyophilized, Liposomes, 6. Unit VII manufactures Tablets, Hard Gelatin Capsules, 7. Unit VII PDII manufactures Tablets, Unit VIII manufactures Hormonal Tablets, Hard Gelatin Capsules, Topical Preparations and Liquid Injectables, 8. Unit IX manufactures Injectables: Liquid and Lyophilized, Prefilled

	Syringes and Liposomes and 9. Unit X manufactures Cytotoxic Tablets, Hard Gelatin Capsules, Soft Gelatin Capsules. The site is dedicated to manufacturing of finished pharmaceutical products. No beta lactams or biological preparations are manufactured on site.
General information about the company and site	CIPLA Ltd. is a public limited company established in 1935. It manufactures and markets a wide range of Pharmaceutical formulations, Active Pharmaceutical Ingredients and Medical devices. Manufacturing sites are situated at different locations in India and abroad. The site at Goa is approximately 25 Km from Panaji, the capital city of Goa and 15 Km from Dabolim Airport. Each manufacturing unit has independent water system, warehouse, technical floor for HVAC systems and Analytical Laboratory. Unit I and IX have independent Microbiology laboratories whereas other units have shared laboratories. More specifically: Laboratory: Serviced to: Unit II Unit II, III and IV Unit V Unit V and X Unit VIII Unit VII, VII PD-II and VIII Stability laboratory of Unit III, IV, VII and VII PD II is shared and located in QC X building. The remaining units have independent stability laboratories. Utilities like compressed air, chilled water and steam are supplied from three shared central blocks. The site draws power from the government grid, with backup provided by generators. Critical operations are supported by UPS (uninterrupted power supply). Potable water is sourced from Industrial Development Corporation and a bore well. This water is used for general purpose and for the purified water generation system. An Effluent Treatment Plant (ETP) is available at the site.
History	The previous WHO inspection was carried out during 13-17 June 2016. Major Changes applicable to all units since the last WHO inspection in 2016: **System related Changes:** Implementation of an Electronic Quality Management System – Deviation, CAPA & Complaint Management Implementation of an electronic management system in Quality Control department Implementation of Track & Trace system to introduce unique serial code for each pack New Supervisory Control and Data Acquisition for Equipment Data Logging & Monitoring System was under implementation at the time of inspection.
Brief report of inspection activities undertaken – Scope and limitations	

<table>
<tr><td>Areas inspected</td><td>Document reviewed including but not limited
Organization Chart
Job descriptions for key personnel
Product Quality Review
Quality Risk Management
Management Review
Responsibilities of the quality units and production
Complaints and Recalls
Deviation control and change control
OOS and investigation
CAPA procedure
Material release
Validation and qualification
Equipment calibration
Data integrity
Sampling and testing of materials
Batch processing records
Materials management system
Purified water system
Sites visited
Unit III – stores, production and packing
Unit IV – stores, production and packing
Unit VII – stores, production and packing and quality control
Unit VII PDII – stores, production and packing
Unit VIII- stores, production, packing, quality control and technical floor
QC X - stability laboratory</td></tr>
<tr><td>Restrictions</td><td>The focus of the inspection included storage, production and quality control areas where WHO Prequalification products were manufactured</td></tr>
<tr><td>Out of scope</td><td>Products not submitted to WHO for Prequalification</td></tr>
<tr><td>WHO products covered by the inspection</td><td>
<table>
<tr><th></th><th>WHO No.</th><th>Product Name</th><th>Manufacturing Unit</th></tr>
<tr><td>1.</td><td>HA039</td><td>Nevirapine Tablet 200mg</td><td>III & (IV, VII)</td></tr>
<tr><td>2.</td><td>HA060</td><td>Lamivudine/Zidovudine 150/300mg tablets</td><td>III & VII (IV)</td></tr>
<tr><td>3.</td><td>HA365</td><td>Lamivudine/ Nevirapine/ Zidovudine 150/200/300mg tablets</td><td>III & VII (IV)</td></tr>
<tr><td>4.</td><td>HA352</td><td>Efavirenz Tablet, Film coated 600mg</td><td>IV & VII</td></tr>
<tr><td>5.</td><td>HA439</td><td>Emtricitabine/ Tenofovir disoproxil fumarate 200/300mg fil coated tablet</td><td>VII & (III, IV)</td></tr>
<tr><td>6.</td><td>HA500</td><td>Efavirenz/ Emtricitabine/ Tenofovir disoproxil fumarate 600/200/300 film coated tablet</td><td>VII & (III, IV)</td></tr>
<tr><td>7.</td><td>HA401</td><td>Tenofovir disoproxil fumarate 300mg</td><td>VII & (III, IV)</td></tr>
</table>
</td></tr>
</table>

		film coated tablet	
8.	HA593	Efavirenz/ Lamivudine/ Tenofovir 600/300/300mg tablets	VII & VII PDII
9.	RH039	Misoprostol tablet 200mcg	VIII
10.	RH040	Levonorgestrel Tablet 750mcg	VIII
11.	RH046	Levonorgestrel Tablet 1.5mg	VIII
12.	HA353	Lamivudine Tablet 150mg	III, IV & VII
13.	MA064	Artemether/ Lumefantrine tablets 20/120mg	III, IV & VII
14.	TB205	Levofloxacin Tablet Film coated 250mg	III, IV & VII
15.	TB227	Levofloxacin Tablet Film coated 500mg	III, IV & VII
16.	HA352	Efavirenz Tablet Film coated 600mg	III
17.	TB228	Cycloserine Capsules 250mg	IV & VII
18.	HA518	Abacavir and Lamivudine 60/30mg	VII
19.	IN013	Oseltamivir PO4 Capsules hard 45mg	VII
20.	IN012	Oseltamivir PO4 Capsules hard 30mg	VII
21.	IN001	Oseltamivir PO4 Capsules hard 75mg	VII
22.	RH030	Ethinylestradiol/ Levonorgestrel + Placebo Ethinylestradiol/ Levonorgestrel Tablet + Placebo tablet 0.03mg/0.150mg+0mg	VIII

Dossier under assessment

HA702	Dolutegravir/ Lamivudine/ Tenofovir disoproxil fumarate 50 mg/ 300 mg/ 300 mg Tablets	VII & VII PD II

Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
APS	Aseptic process simulation
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CFU	Colony-forming unit
CIP	Cleaning in place
CoA	Certificate of analysis
CpK	Process capability
DQ	Design qualification
EDI	Electronic deionization
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis
GMP	Good manufacturing practices

GPT	Growth promotion test
HEPA	High efficiency particulate air
HPLC	High performance liquid chromatography (or high performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
IQ	Installation qualification
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae
MFT	Media fill Test
MR	Management review
NC	Non conformity
NRA	National regulatory agency
OQ	Operational qualification
PHA	Process hazard analysis
PLC	Programmable logic controller
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
RO	Reverse osmosis
SIP	Sterilization in place
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer
WFI	Water for injection

Part 2	Summary of the findings and comments

1. Pharmaceutical quality system

The company had a well-documented pharmaceutical quality system (PQS) with Quality Manual, Corporate Master Documents, Quality Document Guides and Unit Master Documents covering essential GMP principles for the site. Quality assurance (QA) function was involved and had oversight of all activities with impact to product quality. The Quality Manual was presented and was briefly reviewed during the inspection. Senior management responsibilities were well defined. Management review meetings at Unit level were held monthly and the relevant procedure was available during the inspection. The minutes of the previous Unit III management meeting were presented.

Product Quality Reviews

A PQR procedure was in place describing the steps to verify consistency of existing processes, appropriateness of established specifications for starting materials, in process and finished products as well as monitoring trends. PQRs were conducted annually regardless of the number of batches manufactured. A rolling plan for reviewing products was available and timelines for completion of PQRs were set. This plan was prepared by QA personnel and approved by Head QA. If the same product was manufactured in different Units, separate PQRs were prepared and critical process parameters and quality attributes were not compared. 2018 PQRs of products manufactured in Unit III), Unit IV, Unit VII, Unit VIII and Unit VII PDII were checked. Quantitative test results of APIs and excipients, in process results and analytical results of finished product were reviewed and trend analysis was performed as well as calculation of PpK and CpK.

Change Control

There was a corporate procedure for managing changes. Quality risk management principles were incorporated as part of change control process while the impact and proposed action plan were proposed and approved by QA. The scope covered product change requests, document change requests, system change requests, facility change requests, instrument and equipment change requests and any other change request. Changes were categorized into major, moderate and minor. An electronic documentation system was used to manage all changes as well as all documentation at the facility. A matrix for impact assessment of a change was available and instructions on its use were detailed in the change request SOP. Changes were monitored periodically and timelines for completion were set. Their adequacy and effectiveness were reviewed. Examples of change requests were reviewed.

Deviations

There was a corporate SOP for handling deviations. Deviation had to be reported and recorded within 24 hours unless otherwise justified. The procedure was applicable to deviations on manufacturing procedures and processes, documentation, equipment, facility, systems, environmental control, utilities and software. The initiating department was expected to perform root cause investigations, assess impact and recommend appropriate corrective actions. QA was responsible for monitoring and approving relevant documentation. All deviations were expected to be closed within 30 days and there was provision for extension, if justified. Software was used to manage deviations. Deviations were trended by general category as well as by product based and department. Examples of deviation handling were reviewed during the inspection.

Quality Risk Management

Quality Risk Management was applied to different operations across the quality system including but not limited to Deviations, Changes, Product life cycle, Containment. Risk assessment tools were described. The procedure provided for participation of staff from different department when conducting a risk assessment. Several examples of risk assessments were reviewed

2. Good manufacturing practices for pharmaceutical products

Good manufacturing practices generally were well implemented. Necessary resources were provided, including qualified and trained personnel, adequate premises, suitable equipment and services, appropriate materials, containers and labels, approved procedures and instructions, laboratories and equipment for in-process and other controls. Manufacturing steps were recorded in batch manufacturing and packaging records. Manufacturing processes were clearly defined and systematically reviewed. Instructions and procedures were generally written in clear and unambiguous language. Qualification and validation were performed. Operators were trained to carry out procedures correctly, and records were made during manufacture.

3. Sanitation and hygiene

In all the units at site, the level of sanitation and hygiene was generally satisfactory. The company had a standard operating procedure as the basis for its approach to personal hygiene and sanitation in its production facilities. There was appropriate gowning in all areas both for staff and visitors including pictorials and provision for hand sanitization before entry to production areas. In Unit VIII there was provision of wearing pressure suits to protect the operators from hormonal products. Cleaning tools and agents were available. Classified areas were cleaned frequently in accordance with an approved written programme.

4. Qualification and validation

Protocols and reports were in place for qualification and validation. A Validation Master Plan existed. The key elements of a qualification and validation programme were defined. Documentary evidence was available that the premises, supporting utilities, equipment and processes were designed, installed, operated in accordance with their design specifications. Qualification of a compression machine (Unit VII PDII) was reviewed. Similarly, qualification of the containment box used for sampling and dispensing (Unit VIII) was checked. The Unit VIII technical floor where AHUs were installed, was visited and spot checks on AHU maintenance, cleaning and requalification were made. Cleaning validation in Unit VII followed an approved procedure. The worst-case scenario was determined by taking into account solubility, potency and toxicity of the products as well as the equipment used. Toxicologic reports and determination of PDE values followed an approved procedure. Toxicologic reports were prepared by Cipla personnel possessing appropriate qualifications as indicated by reviewing their CVs. Toxicologic reports were reviewed every 3 years. It was noted that certain toxicological reports included limited toxicologic references and the procedure did not clearly define how PDE values could be derived in case sufficient toxicologic data was not available. Identified observations were appropriately addressed and closed out in the CAPA plan.

5. Complaints

There was a procedure in place for handling product complaints, which provided for a risk based classification as minor, major or critical. Complaints were initially received by Corporate QA and after a preliminary investigation they were forwarded to the relevant site/unit. Complaints were managed using appropriate software. Timelines for investigation of a complaint were established, if a complaint could not be closed out within the set timelines a reason for extension had to be provided. There was trending of the complaints every 6 months and the trends for June-December 2018 were reviewed.

6. Product recalls

A procedure for handling product recalls was available. Three classes were defined according criticality and urgency of recall. The procedure also adequately described the depth of recall and the decision-making process. The recall decision was made by the Head of Global Quality Compliance and the Global Alignment Group was responsible for classifying the recall and deciding the depth (e.g. consumer level, wholesaler level). Mock recalls were conducted every two years if no recall had been conducted in between. The Class II recall of a product initiated in December 2018 was reviewed.

7. Contract production, analysis and other activities

Manufacturing and analysis of WHO prequalified products was not contracted to any third party.

8. Self-inspection, quality audits and suppliers' audits and approval

Self-inspections were performed according to a documented procedure. The SOP described in detail the composition of the audit team, the classification of the findings (critical, major, minor, data integrity related) and specific timelines for the finalization of audit report and the response time of the auditee according to the criticality of the findings. The responses were evaluated from the audit team. The different units were categorized according to risk rating criteria. The implementation of the self-inspection procedure was reviewed.

Vendor Approval

There was a procedure in place for selection, evaluation and approval of API manufacturers. Potential suppliers were identified by supply chain department in consultation with R&D. Evaluation and approval of a supplier was performed by corporate QA. Both site audit and documentation evaluation were used in the qualification process. In addition, for API suppliers process validation and 3-month stability data were taken into account. Re-evaluation and certification of approved manufacturers was described in a written procedure. A risk priority number (RPN) was established and audit frequency was assigned based on this calculation. There was provision to disqualify a supplier if the RPN number was above a certain limit on two consecutive evaluations or if no material was procured from that manufacturer for three years. Examples of requalification of suppliers were checked.

9. Personnel

There were more than 3900 staff working at Cipla Ltd., Goa while approximately 1930 employees were working in the Units inspected. Key personnel's specific duties were recorded in written job descriptions. The detailed duties of the compression department manager, deputy manager and assistant manager for unit III were reviewed, covering adequately the assigned duties and responsibilities. The general organogram of the site was reviewed. This organogram was further divided in unit level. The organogram from UNIT III, for QA department, for Quality Control department and Production department were reviewed. The organogram depicted accurately the organization and the relation between different department and the different managerial levels.

10. Training

There was a training procedure available. It applied to both permanent and contract workers. The SOP adequately described the induction training of new recruits and scheduled training. Induction training included introduction to quality policy, company policies, company practices and procedures, procedures in safety, personnel hygiene, GMP and data integrity issues. On the job training program was issued from the head of the department where the new recruit was assigned. After completion of training on each identified subject, the incumbent was evaluated from three reviewers, and if successful a certificate was issued. Trainers and reviewers were qualified, and the list of certified trainers was made available. The scheduled training was performed according to an annual program which was compiled according to identified training needs. The implementation of the training SOP for new recruits and for planned training was reviewed. Given the large number of employees at site, it is strongly recommended to adopt an electronic system for managing training activities at site.

11. Personal hygiene

There was a procedure in place detailing health and hygiene principles. The sanitation and hygiene measures in place at the time of the inspection were found to be adequate ensuring prevention of contamination and maintenance of cleanliness. Applicable procedures relating to sanitation and hygiene were available at the site of activities or workstation. All changing rooms were provided with documented and depicted procedures describing the gowning procedures. Mirrors were available to check on the gowning before entering in the production areas. There was also provision for hand sanitisation after gowning. In Unit VIII where sex hormone products were manufactured, no women were allowed to work and there was provision of using a positive pressure suit to protect operators. In addition, there was a procedure in place that provided sufficient instructions on avoiding cross-contamination. Personnel working in Unit VIII was not allowed to enter any other Unit in the same day. Pre-employment medical examinations as well as annual medical examinations were foreseen for both permanent and contract personnel. Personnel working in Unit VIII had to undergo medical examination every 6 months. Records of periodic medical examinations for personnel working in Unit VIII were made available.

12. Premises

Generally, premises were located, designed, constructed, adapted, and maintained to suit the operations being carried out. The design of premises was logical and laid out in a manner to minimize the risk of errors and cross-contamination and permit effective cleaning and maintenance. The production area was laid out to allow production to take place in areas connected in a logical order corresponding to the sequence of the operations and to the requisite cleanliness levels. Exposed surfaces were smooth, impervious and unbroken to minimize the shedding or accumulation of particles or microorganisms and permitted the repeated application of cleaning agents and disinfectants, where used. Changing rooms were flushed with filtered air. Changing rooms were designed as airlocks and used to provide physical separation of the different stages of changing. Changing rooms were equipped with mirrors. Airlock doors were interlocking. There were two central warehouses adjacent to the area where the manufacturing units were located. Each Unit had its own warehouse area to accommodate production needs. A detailed floor layout for each Unit was made available.

Unit-III: The ground floor for Unit-III included quality operations and laboratory, raw materials and packing materials warehouse and ancillary areas; while the first floor included production, packaging and water utility section and technical area. There was also a service floor available

Unit-IV: The ground floor included materials and finished products stores, sampling and dispensing areas and ancillary areas; while the first floor included: production and packaging areas.

Unit-VII: The ground floor included materials and finished products stores, dispensary, production, packaging and water utility section as well as ancillary areas. The first floor was largely occupied by the technical area. Some production and packaging rooms as well as the laboratory and some ancillary areas were also located on the first floor. The second floor included the service area, clean equipment stores and water utility section.

Unit-VII PDII: The ground floor included materials and finished products stores and packaging areas as well as ancillary areas. The QC laboratory, personnel change rooms as well as service areas were located on the first floor. The second floor included production areas and the third floor included technical areas and HVAC.

Unit VIII (hormones): The ground floor included materials and finished products stores, change rooms, dispensary, production areas for solid and, packaging as well as ancillary areas. Topical and sterile products were manufactured on the first floor. The microbiology laboratory and water system were located on the second floor. Quality control and stability chambers were located in building QCX.

13. Equipment

Equipment in the premises was installed in a logical way to accommodate manufacturing processes. It was generally maintained in a good state of repair and each piece of equipment had a unique identification number. Calibration and preventive maintenance labels were placed on each critical equipment including balances and pressure gauges. They were found to be within the validity timelines for calibration and maintenance. Procedures for cleaning of each piece of equipment were available in the production area and records were maintained. There were separate log books kept for cleaning, usage and preventive maintenance of each equipment. The pipework for potable and purified water were labelled and the direction of flow was indicated.

14. Materials

Raw materials were sourced from approved sources and necessary checks were done at the procurement stage as well as during receipt. The procedure on receipt of materials and relevant documentation were checked during the Unit III visit. Labels for raw materials were generated by software which was bridged with the material management system. In case of damaged labels there was a procedure in place describing reprinting of labels; this process required approval by QA. Starting materials were stored under appropriate conditions of temperature and humidity which were monitored and controlled. Received materials were quarantined, sampled and analysed before they could be used for production. Stock management was through the material management system and there were enough personnel to handle stores operations. Raw material sampling and dispensing were done at appropriate cleanliness classification. Hormone APIs were dispensed in an isolator in Unit VIII.

15. Documentation

There was a procedure in place for documentation control. The procedure provided adequate details on the process of implementing procedures coming from corporate level. In addition, there was a procedure in place for the preparation of SOPs. Procedures at site were electronically managed by an electronic documentation management system. In general, records and procedures followed approved formats and were dated and signed by responsible persons. Most of the SOPs for the quality management system were written at corporate level and adopted by each unit. This ensured a homogenous QMS across units and other sites.

16. Good practices in production

All manufacturing units were visited. Floor plans were provided during the visit. Areas inspected included storage rooms, dispensing areas, granulation, compression rooms, coating rooms and primary and secondary packaging areas as well as the technical floor of Unit VIII. The production areas and equipment were kept in a good cleanliness level and were appropriately maintained. Temperature and humidity conditions as well as differential pressure between production rooms were controlled and monitored by BMS. Rooms and equipment were appropriately labelled. Dusters and metal detectors were dedicated to compression machines. Line clearance was performed before introducing a new batch. Personnel entered production areas through appropriate change rooms. BMRs and BPRs of batches being manufactured during the tour were spot checked as well as maintenance and calibration of equipment. sanitation and hygiene.

17. Good practices in quality control

Quality control operations were separated from production. In general, analytical and microbiology laboratories visited had appropriate equipment and utilities and the premises were appropriately maintained. Specifications for materials were maintained and were easily retrievable. Logbooks for use and maintenance of equipment were available. Spot check on qualification of equipment were made (e.g dissolution apparatus Unit VII). Retained samples were appropriately maintained in accordance with a written procedure. Software was used for managing samples of materials while reference standards were managed by a different system. Procurement of reference standard was done at corporate level. There were appropriate refrigerators for storage of reference standards. Traceability on use of the reference standards was maintained.

There was a procedure in place for registering and investigating OOS results. The procedure included detailed steps for the investigation of this type of results. Examples of OOS investigations were reviewed and did not raise any observations

Stability Chambers and QC laboratory for Unit VIII were located on the 2nd floor of building QCX. Stability laboratory of Unit III, IV, VII and VII PD II were located on the first floor of building QCX. There were 15 walk-in stability chambers installed on the second floor for evaluation of product stability at various conditions of temperature and humidity. Software was used to monitor the chambers. Alarm mode was checked every day. Audio alarms were installed in the engineers' room who were operating 24hrs/day. Stability samples had to be withdrawn within 3 days of the target date and analyses had to be completed within 30 days from the withdrawal date.

Part 3	**Conclusion – Inspection outcome**

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, ***Cipla Ltd,*** located at ***Plot No L-139 to L-146, S-103 to S-105, S-107 to S-112, L-147. L-147/1 to L-147/3, L-147/A & L-138 & M-61 to M-63, Verna Industrial Estate, Salcette, Goa, 403 722, India***was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines.

All the non-compliances observed during the inspection that were listed in the full report as well as those reflected in the WHOPIR, were addressed by the manufacturer, to a satisfactory level, prior to the publication of the WHOPIR

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.

Part 4	**List of WHO Guidelines referenced in the inspection report**

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO TRS No. 986, Annex 2***
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/
2. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2. ***Short name: WHO GMP for APIs*** or ***TRS No. 957, Annex 2***
   http://www.who.int/medicines/publications/44threport/en/

3. WHO good manufacturing practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourth-Sixth Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2
   Short name: WHO TRS No. 970, Annex 2
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/
4. WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-Ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4
   Short name: WHO TRS No. 929, Annex 4
   http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1

5. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8. **Short name: WHO TRS No. 1010, Annex 8**
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_1010/en/

6. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4
   Short name: WHO TRS No. 937, Annex 4
   http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf?ua=1

7. WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1
   Short name: WHO GPPQCL Guidelines or ***TRS No. 957, Annex 1***
   http://www.who.int/medicines/publications/44threport/en/

8. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2
   Short name: WHO TRS No. 957, Annex 2
   http://www.who.int/medicines/publications/44threport/en/

9. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 6
   Short name: WHO TRS No. 961, Annex 6
   http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7
Short name: WHO TRS No. 961, Annex 7
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

11. Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 9. ***Short name: WHO TRS No. 961, Annex 9***
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

12. General guidelines for the establishment maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-First Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3
Short name: WHO TRS No. 943, Annex 3
http://whqlibdoc.who.int/trs/WHO_TRS_943_eng.pdf?ua=1

13. WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2
Short name: WHO TRS No. 961, Annex 2
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

14. WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2. ***Short name: WHO TRS No. 981, Annex 2***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

15. WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3. ***Short name: WHO TRS No. 981, Annex 3***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

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