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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	**Ipca Laboratories Limited, Pithampur – Hormone**
Corporate address of manufacturer	Ipca Laboratories Limited Building No.: 125, CTS No.: 328, Kandivli Industrial Estate, Kandivli (West) Mumbai, Maharashtra, 400 067, India
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Ipca Laboratories Ltd, Plot No. 470, 471 & 481, Sector – 3, Industrial Area, Pithampur, Dist. Dhar, Madhya Pradesh, 454 775, India
Unit / block / workshop number	Hormone plant
Inspection details	
Dates of inspection	12-15 March 2019
Type of inspection	Initial GMP inspection
Introduction	
Brief description of the manufacturing activities	Ipca's manufacturing facility for hormone formulation is located at Plot No. 470, 471, 481, Sector – 3, Pithampur Dist. Dhar (M.P.), India. The Ipca's Hormone site was incorporated in 2011 with the present management taking it over in 2014. The site employees 48 staff.
General information about the company and site	Ipca Laboratories Limited was initially incorporated in 1949. The present management has taken over the company since 1975 and has around 13,000 employees. It is one of the leading Pharmaceutical Company in India, with manufacturing activities in the areas of Pharmaceutical Dosage Forms, Active Pharmaceutical Ingredients (API) and Drug Intermediates. Ipca has multiple facilities located at Pithampur – Sector 3 (Hormone Plant), SEZ-Indore (Pithampur), Piparia, Kandla, Ratlam, Athal, Sikkim, Dehradun, Tarapur, Aurangabad, Ranu, Nandesari, Ankleshwar, Indore and Mahad allowing for the manufacture of a wide range of products.

History	This was the first WHO PQ inspection as well as the first international inspection of Ipca's Hormone site based in Pithampur. From the opening meeting presentation, it was noted that the site was jointly inspected by the State FDA and CDSCO in June 2018.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Document Review included but not limited to: - Documentation system - Semi-finished & finished product testing and release - Job descriptions - Self-inspection - Change control - Annual product quality review - Deviation control - OOS, OOT, and investigation - Handling of laboratory events - Good analytical and review practices - Process validation and continued process verification - Cleaning validation - Quality risk management - Batch manufacturing records - Specifications and method of analysis - Computer system validation - Stability studies - Validation master plan - Electronic data and audit trail **Site areas visited:** - Manufacturing area covering granulation, compression, packing; - QC laboratories including chemical and microbiological; - Purified water system - Service floor (air handling units) -
Restrictions	None
Out of scope	None
WHO products covered by the inspection	Norethisterone Tablet 0.35mg tablet (RH088)

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 has established a quality management system based on the requirement of national and international regulatory authorities. The quality and production departments operate independently under different leadership. Senior Management demonstrated a commitment to the QMS by granting adequate resources to implement, support and manage the QMS. Senior management also participates in the system through the conduct of periodic management review meetings, discussion of PQR`s and the PQS itself.

The quality assurance department was responsible for the batch release of the finished pharmaceutical products whereas quality control department ensures approval/rejection of incoming starting and packaging materials and final release in SCM by quality assurance department. The QA reports to corporate QA based in Mumbai whereas QC reports to the Unit Head.

The process development, analytical method development, validation, and verification was conducted at the same site using a separate set of equipment and instruments.

The quality management and quality control functions were supported by IT software:

- GMP critical computerized system consists of Chromatographic data system (CDS) and Non-Chromatographic data system (Non-CDS) associated with laboratory instruments (Empower-3).
- Inventory of the materials, their documentation, and the release process are controlled through Supply Chain Management (SCM).
- Generation of corporate standard operating procedures (CSOP), Specifications for Starting Materials, Intermediates and Finished Goods and their revisions is with Corporate Quality Assurance (CQA) and approved specifications through Document Management System (DMS).
- Change control, deviations, investigations, and CAPA on TrackWise
- Learning Management System (LMS) is planned to be implemented

- Laboratory Information Management System (LIMS) is planned to be implemented
- PLC/HMI based production equipment and water system
- LES implemented on Ipca's three manufacturing locations (serving to US markets)

Laboratory incidents, OOS, market complaints are handled manually.

Product quality review (PQR)

Product quality review was discussed. The procedure included a review of complaints, recalls, return, OOS, starting materials, primary packaging, APIs, critical excipients, analytical parameters, in-process control results, manufacturing & packing process, finished product analysis, and other aspects. The review was performed on a calendar and rolling year basis.

The SOP on **data reliability** was discussed. The procedure defined the control and initiatives which should be in place to ensure the integrity of data. The procedure was applicable to all GXP operations. The procedure defined ALCOA principles as well as improper practices such as deletion of noncompliant data, improper peak integration, fabrication/falsification of records etc. The procedure was supported with annexures (improper practice reporting form, review comment form and data integrity concern record log).

Management quality review meeting/MQRM procedure was discussed. The corporate quality assurance (CQA) was responsible for the implementation of this procedure. Respective department heads were invited to Ipca's Head Quarter in Mumbai for a quarterly meeting. The meeting is chaired by the President of Technical Operations, Corporate Quality, and Executive Director. The minutes of the meeting was recorded. The last management review meeting was held on 19th Feb 2019 and action points were discussed and documented.

Change controls

The change control activities were covered by two procedures. The SOP 'Handling of change control proposal' is the basic procedure concerning change controls. Additionally, the SOP covers changes which are handled manually and are still in progress.

Quality risk management (QRM)

According to the procedure, QRM covered systematic processes designed to coordinate, facilitate and improve science-based decision making with respect to risk. Few tools such as FMEA, FMECA, FTA, PHA were used for the assessment of risk. Risk assessment pertaining to the requalification of equipment and instrument was reviewed. Some weaknesses were observed.

Corrective actions and preventive actions (CAPA)

The CAPA activities were covered by two procedures. The SOP 'Corrective Action and Preventive Action' is the general procedure which covered handling of manually. The SOP 'Handling CAPA in TrackWise Software' is applicable for the handling of CAPA in TrackWise software.

Batch release

The Annexure 2 of the SOP 'Procedure for Release of Batch dispatch' stipulated the use of "Checklist for auditing of Batch record and release of batch". Annexure 1 contained a form for batch certification/ batch release 'Certificate of conformance'. The term qualified person (QP) was not defined in the procedure.

The release of starting material and packaging material

According to the 'Procedure for approval/rejection of raw material and packaging material', Head of QA was responsible for the final release or reject of raw material and packaging material.

The deficiencies raised from this section have been satisfactorily addressed through submission of CAPAs, and the same shall be verified during routine inspections.

2. Good manufacturing practices for pharmaceutical products

Basic principles of good manufacturing practices were described and implemented. Manufacturing processes were generally adequately defined and documented in BMRs and BPRs. Required resources were available, including adequate premises, equipment, and utilities. Appropriately qualified personnel were employed.

Although commercial production from Ipca's this facility has not started yet, the production facility is a multi-product / shared facility. It is a small production facility equipped with a minimum number of production and packaging equipment most of them were not operational at the time of inspection. It was noted that some of the manufacturing equipment are not equipped with an online camera inspection system, 2D bar code etc. The company has committed to installing this equipment before the commercialization of Norethindrone tablets.

3. Sanitation and hygiene

Premises and equipment were generally cleaned according to established procedures. Change rooms were well maintained and authorized instructions displayed the steps and dress code. Cleaning records of manufacturing rooms and equipment were in place.

4. Qualification and validation

The qualification/validation programs were designed to evaluate the manufacturing process and process equipment to assure quality and cGMP compliance. Qualification programs of area and equipment's were performed periodically to ensure the suitability of area and equipment. Validation programs were established to verify and document the ability to attain reproducible results during manufacturing, packaging, testing and cleaning operations.

Validation master plan for Ipca's Pithampur Hormone Sector-3 was discussed. The VMP provided a conceptual approach to validation and systematic approach on validation program. The VMP covered qualification of equipment & facility, validation of the processes (process, packaging, cleaning, analytical method, computerised system, personnel qualification, vendor qualification and more. In addition to the VMP which provided company' philosophy on validation activities, the VMP was supported with corporate SOPs (process validation, computer system, cleaning and more).

Process validation protocol and report of Norethindrone tablets USP 0.35mg were discussed. Three batches were manufactured as part of the process validation study.

Cleaning validation procedure provided the strategy and procedure for cleaning validation. When exhibit (process validation) batches of Norethindrone tablets were produced in 2017. The company has purchased the permissible daily exposure (PDE) and occupational exposure limit (OEL) data from an independent supplier, however, these PDE and OEL values have not been considered for the cleaning validation studies.

A corporate procedure on equipment, system and facility qualification was briefly reviewed. It was noted that periodic requalification was performed based on an annual review of critical equipment.

According to "Microbiological examination of non-sterile material – Levonorgestrel tablets USP 1.5 mg – validation protocol", the validation of the analytical method of Escherichia coli was performed. Raw data were verified. The growth promotion test of the media which was used in validation of the analytical method was done in accordance with the SOP 'Procedure for Media Management').

The deficiencies raised from this section have been satisfactorily addressed through submission of CAPAs, and the same shall be verified during routine inspections.

5. Complaints

The SOP 'Handling of Product Complaint' was applicable for products complaints received from the customer, market, pharmacy, and regulatory authority. According to the SOP, the complaint can be related to manufacturing, packing, adverse drug reaction, purity, safety, efficacy and quality of drug product manufactured in Ipca Laboratories Ltd. The Head of QA was responsible for the final classification of the complaint and review of complaints. Furthermore, the head of QA investigates the product complaint and reports critical finding to CQA for assessment. After evaluation, CQA informs the regulatory agencies. According to the SOP, each complaint should be closed in 30 days. There were no complaints during 2018.

The deficiencies raised from this section have been satisfactorily addressed through submission of CAPAs, and the same shall be verified during routine inspections.

6. Product recalls

The SOP 'Product Recall – export market' was applicable for drug products manufactured by Ipca Laboratories Ltd for all export markets. The SOP 'Product Recall – domestic market' was applicable for drug products manufactured by Ipca Laboratories Ltd for the domestic market. According to the SOPs, the final decision concerning the recall of the medicinal product remains the responsibility of the Managing Director of Ipca Laboratories Ltd. As specified in the SOPs, "mock recall" will be carried out as soon as the commercial production is started. Mock recall of the other manufacturing site of Ipca Laboratories Ltd. Was present during the inspection.

The deficiencies raised from this section have been satisfactorily addressed through submission of CAPAs, and the same shall be verified during routine inspections.

7. Contract production, analysis and other activities

Ipca Pithampur (Hormone plant) does not outsource the manufacturing of any product to third parties. Although it was indicated by the company that the quality control laboratory is self-sufficient to carry out most of the tests in-house, some testing activities are contracted to a third-party laboratory certified by NABL / Local FDA Authorities such as Atomic Absorption spectroscopy, Particle size etc.

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

The SOP 'Self-inspection' covered among others, Manufacturing Department, QA Department, and QC Department. Qualifications of auditors and rules and responsibilities were defined. As per the SOP, the frequency of self-inspections was set to at once in six months. Furthermore, unannounced self-inspection may be performed. The schedule for the current year was prepared at the end of the previous year. Classification of deficiencies was defined.

The deficiencies raised from this section have been satisfactorily addressed through submission of CAPAs, and the same shall be verified during routine inspections.

9. Personnel

Responsibilities of staff and their specific duties were recorded in written job descriptions. Personnel interviewed during the inspection were aware of the principles of GMP in general. Organization charts and job descriptions were available.

The staff component of the company was as follow:

Sr. No.	Department	No. of Employees
1	Production and Packing	7
2	Engineering	7
3	HR and Admin	2
4	Warehouse	2
5	Quality Control	6
6	Quality Assurance	7
7	PDR	5
8	ADL and AMV	9
9	Purchase	1
10	IT	1
11	EHS	1
	Total	**48**

The deficiencies raised from this section have been satisfactorily addressed through submission of CAPAs, and the same shall be verified during routine inspections.

10. Training

The SOP 'Procedure for Training of plant personnel' was discussed which described procedure for employees training. Following types of training was provided, on-job training, schedule training, external training, self-reading training and incidental training. As stated under "Yearly Schedule Training calendar 2019", two training per month was planned.

The deficiencies raised from this section have been satisfactorily addressed through submission of CAPAs, and the same shall be verified during routine inspections.

11. Personal hygiene

Personnel gowning procedure was appropriate and was generally followed. Personnel was medically examined before offered a contract and then annually. Human resources were responsible for monitoring the medical examination program and maintain relevant records. The SOP 'Procedure for Personal Hygiene Practices' stipulated the hygienic practises, ways of dealing with infection or skin disease, medical examination, working rules in the production area.

12. Premises

The premises are comprised of the following manufacturing areas:

Manufacturing Areas	
Sex Hormone Area	Manufacturing of female Sex Hormone Tablets
Non-Sex Hormone Area	Provision for manufacturing of Non-Sex Hormone Tablets
Ferrous Area	Provision for manufacturing of Ferrous Tablet

Manufacturing areas
All core process areas are designed to maintain the cleanliness level as per ISO Class 8 (Class 100,000) at rest condition (Sampling, Dispensing, Granulation, Compression, Coating, and Primary Packing area). Sampling and Dispensing areas are provided with Isolator for API sampling and Dispensing and Reverse

Laminar Airflow Work Stations (RLAF) for containment of dust. All storage area is designed to maintain a controlled environment condition as per the requirement (Raw material, Primary packaging material, Secondary Packaging Hall, Finished Goods Store). Surrounding corridors and passages are ISO 8 (Class 100,000) at rest condition and maintained at positive air pressure gradient with respect to all processing areas.

QC areas
QC laboratories were separated from production areas. The laboratories have been designed and equipped with facilities for chemical, instrumental, microbiological and stability testing.

Storage areas
The storage areas were of sufficient capacity to allow orderly storage of various categories of materials such as starting and packaging materials, finished products, products in quarantine, released products, rejected and returned products. Receiving and dispatch bays were separated and protected materials and products from the weather. A printed packaging material was stored in accessed control areas.

HVAC is located on the service floor of the Manufacturing Plant. The sequence of filtration of supply air in the facility includes accessories of filters with 10µm pre-filter, 3µm &1µm fine filter and finally passed through a 0.3µm terminal HEPA filter. Return air raiser with 10µm, 0.3µm filter installed in processing area for pick up air at low level. Clean unclassified (CNC) design are considered other than processing area e.g. warehouse secondary packing and outer corridor. The air changes rate in the processing area is a minimum of 20 air changes per hour (ACPH). The HVAC system is designed for 85% re-circulation and 15 % fresh air.

Water Purification system is in the manufacturing block & utility block with the Boiler and Air Compressor located in a separate building in the Utility Block. For a generation of purified water, source water is passed through MGF → Softener→ UF→RO → EDI and collected in the purified water storage tank. The purified water generation capacity is 500 litre per hour and a purified water storage tank has a capacity of 1200 litre. A recirculation loop system is designed for the distribution of purified water to end user. UV is installed in the supply line of the loop. For controlling microbial growth periodic heat sanitization is carried out of purified water storage and distribution loop system.

The deficiencies raised from this section have been satisfactorily addressed through submission of CAPAs, and the same shall be verified during routine inspections.

13. Equipment

The equipment used in the manufacturing, processing, and packaging was of appropriate design, adequate size, and complying to cGMP norms. The equipment was placed in a suitable location to facilitate operations for their use, cleaning, and maintenance. Validation of the laboratory instruments and software was performed.

The SOP for the procedure for operation, calibration, verification, and cleaning of electronic & analytical weighing balances was discussed. The balances were calibrated once every year by an external party whereas verification of balances was performed in-house monthly. The calibration included repeatability, eccentricity and linearity test. From the review of the calibration report performed by Rachna Cooperation for balance, the calibration did not cover the operating range. Similarly, daily verification did not cover the entire operating range. It was noted that there was no technical agreement available between Ipca Laboratories and Rachna Cooperation as work was performed based on the purchase order.

The production department was responsible for the calibration and requalification of production equipment whereas the maintenance/engineering department was responsible for preventive maintenance of production equipment including calibration of pressure gauges and utility equipment.

The deficiencies raised from this section have been satisfactorily addressed through submission of CAPAs, and the same shall be verified during routine inspections.

14. Materials

The warehouse was briefly visited. Incoming materials (active, excipients, packaging materials) were received through the receiving bay. The receiving bay was equipped with trap station used for rodent bait. After the dedusting activity, containers were verified for weight. Two balances were used for weight verification. Supply chain management (SCM) system was used for materials management.

Separate sampling & dispensing was performed for active substances, excipients, packing materials, and solvents. During the visit to the warehouse it was observed that API store area housed materials under different status (undertest, quarantine, approved and rejected), however materials of different status were not physically segregated. In fact, Norethindrone and Levonorgestrel were stored together without physical segregation.

Sampling and dispensing of active substances were carried out under the isolator claimed to be negatively pressurized. The isolator had three chambers (transfer of canister, main compartment and for waste management). Dispensing was performed by the warehouse in the presence of production executive and QA.
The deficiencies raised from this section have been satisfactorily addressed through submission of CAPAs, and the same shall be verified during routine inspections.

15. Documentation

Site documentation was controlled by the Quality Assurance Department. The users of the individual departments prepare procedures (SOPs) in standard format as per the SOP for SOP Writing. Site documentation control system procedure was in place describing the preparation, checking, authorization, controlling of documents and distribution. Quality Assurance was responsible for controlling and distribution of documents. Master documents were stored in the Documentation room having access control and lock and key.

The deficiencies raised from this section have been satisfactorily addressed through submission of CAPAs, and the same shall be verified during routine inspections.

16. Good practices in production

The production area was further divided into a production area for sex (in operation) and non-sex (no operation) hormone, ferrous area (no operation) and warehouse (in operation). Adequate gowning (shoe covers, hairnet, pressure suits, hand gloves) and personnel protective equipment (3M nose mask) were provided for the visitors as well as for the staff before entering the core processing areas and their respective corridors. The different colour uniform was provided for personnel working in the dispensing, granulation, coating and packing.

At the time of the inspection, a demonstration batch for Levonorgestrel Tablets BP 0.75 mg (Batch No. IAJ190019) was being produced. The production area was equipped with the following area/equipment:

- one dispensing area with isolator for API
- one dispensing area with RLAF for excipient
- two granulation areas of different capacity (one area used)
- one blending area
- one compression area (provision for two available)
- one coating area (provision for three available)
- one inspection area and
- one blister machine (provision for three available)

The manufacturing area was classified as Grade D (ISO 8) wherein differential pressure was maintained as follows:

- 40 Pa (corridor)
- 25 Pa (airlocks)
- 15 Pa (core processing areas)
- 5 Pa (shower upon existing)
- 15 Pa (buffer area)
- 25 Pa (material airlock)

The deficiencies raised from this section have been satisfactorily addressed through submission of CAPAs, and the same shall be verified during routine inspections.

17. Good practices in quality control

The site has its own quality control laboratory (QCL) comprising of different sections such as Raw Material Analysis, Packaging Material Analysis, In-process, Finished Product Analysis, Microbiology, and Stability testing. QCL is equipped with several technical and support staff in each section. The laboratory is equipped with commonly used and sophisticated analytical testing instruments and equipment.

The laboratory was equipped with the following equipment:

- 4 HPLC Waters make connected to Empower 3.0
- 1 GC Perkin Elmer connected to Empower 3.0
- 1 FTIR Brooker / OPUS
- 1 UV-VIS Shimadzu / UV-Probe
- 2 balances

The laboratory had 4 analysts and 2 microbiologists. A separate laboratory adjacent to the main laboratory was responsible for analytical method development and validation.

The Microbiological Laboratory was in the QC area. All microbiological tests of medicinal products, APIs, PW and all activities related to microbiological monitoring were carried out there.

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, ***Ipca Laboratories Ltd, Hormone Plant***, located at ***Plot No. 470, 471 & 481, Sector – 3, Industrial Area, Pithampur, Dist. Dhar, Madhya Pradesh, 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/

16. WHO guidelines for drafting a site master file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 14. ***Short name: WHO TRS No. 961, Annex 14***
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

17. WHO Guidelines on good manufacturing practices: validation, Appendix 7: non-sterile process validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 3. ***Short name: WHO TRS No. 992, Annex 3***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

18. WHO General guidance on hold-time studies WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4. ***Short name: WHO TRS No. 992, Annex 4***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

19. WHO Technical supplements to Model Guidance for storage and transport of time – and temperature – sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 5. ***Short name: WHO TRS No. 992, Annex 5***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

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