

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

Part 1	General information
Manufacturers details	
Company information	
Name of manufacturer	Mylan Laboratories Limited (Hosur Sterile Facility / HSF)
Corporate address of manufacturer	1000 Mylan Blvd, Canonsburg, PA, 15317 USA
Inspected site	
Address of inspected manufacturing site if different from that given above	Hosur Sterile Facility, Plot # 14, Sipcot-II , Krishnagiri Main Road, Hosur- 635109 Tamil Nadu -India II : +91-4344 -661400 - +91-4344 - 661499
Unit / block / workshop number	N/A
Manufacturing license number, (delete if not applicable)	TN00003234
Inspection details	
Dates of inspection	9-13 January 2017
Type of inspection	Initial GMP inspection
Introduction	
Brief summary of the manufacturing activities	The dosage forms manufactured and the corresponding product lines are as follows: – Sterile liquid Parenteral in vials, aseptically filled (2-50 ml), Bosch line – Sterile liquid Parenteral in vials, terminally sterilized (1-50 ml), Bosch line – Sterile lyophilized Parenteral in vials (5-30 ml), Combi line-Lyo – Sterile liquid Parenteral in Ampoule (1-10 ml), Ampoule line – Sterile liquid Ophthalmic products (5-15 ml), Ophtalmic line (existing, not used), Combi line No other manufacturing activity is carried out at the site. No routine production has happened in the Combi line-Lyo since the accomplishment

	of the remediation (May 2016). The only commercial production was 4 batches of a lyophilized product (for non-WHO market). The site runs in three shifts (including production and QC), it employed total of 401 staff excluding the housekeeping staff primarily working in non-critical areas as confirmed by the site management. Capreomycin powder injection was produced on a non-dedicated line. Production planning for the week was discussed. The site decided to run the lyophilized product using 5ml vial on Combi line-Lyo during the inspection, claiming that filling of small volume vial is more challenging than large volume.
General information about the company and site	Mylan Laboratories Limited. Hosur Sterile Facility, Tamil Nadu is dedicated for sterile products mainly for the US market. The total area of the site is about 2 acres; the constructed area is about 13650 sq. Meter (Ground floor - 5325 sq. mts, 15t floor - 5110 sq. mts and Basement - 3000 sq. mts).
History	The facility was acquired by Mylan from Agila specialties Pvt Ltd. in 2013. Agila acquired Star Drugs and Research Labs in 2012. The manufacturing facility had been approved by Tamil Nadu Drugs Control Department (located at Chennai, India). The drug manufacturing license number: TN00003234 (for the manufacture of small volume Parenteral). The manufacturing site was inspected by the US FDA in 2013. There was a voluntary shutdown (remediation and upgradation) program initiated on in February 2015 which has ended on May 2016 including the following major changes: – new vial filling and sealing machine – new terminal sterilizer, – new steam sterilizers (3 numbers) – <i>new manufacturing reactor (1000L) and a filtration vessel (1000L).</i>
Brief report of inspection activities undertaken	
Scope and limitations	
Areas inspected	– Pharmaceutical quality management system – Validation and qualification – Quality control, chemical – Quality control, microbiology – Material management – Production (Combi line-Lyo) – Personnel
Restrictions	N/A
Out of scope	The product lines not involved in the production of the lyophilized products were out of the scope.

WHO product numbers covered by the inspection	TB 329, Capreomycin 1g powder for injection (lyophilized)
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Abbreviations	AHU	air handling unit
	ALCOA	attributable, legible, contemporaneous, original and accurate
	API	active pharmaceutical ingredient
	APQR	annual product quality review
	BDL	below detection limit
	BMR	batch manufacturing record
	BPR	batch packaging record
	CAPA	corrective actions and preventive actions
	CC	change control
	CFU	colony-forming unit
	CoA	certificate of analysis
	CpK	process capability index
	DQ	design qualification
	EM	environmental monitoring
	FAT	factory acceptance test
	FBD	fluid bed dryer
	FMEA	failure modes and effects analysis
	FPP	finished pharmaceutical product
	FTA	fault tree analysis
	FTIR	Fourier transform infrared spectrometer
	GC	gas chromatograph
	GMP	good manufacturing practice
	HACCP	hazard analysis and critical control points
	HPLC	high-performance liquid chromatograph
	HVAC	heating, ventilation and air conditioning
	IR	infrared spectrophotometer
	IQ	installation qualification
	KF	Karl Fisher
	LAF	laminar air flow
	LIMS	laboratory information management system
	LoD	limit of detection
	LOD	loss on drying
	MB	microbiology
	MBL	microbiology laboratory
	MF	master formulae
	MR	management review
	NMR	nuclear magnetic resonance spectroscopy
	NRA	national regulatory agency
	OQ	operational qualification
	PHA	process hazard analysis
	PM	preventive maintenance
	PpK	process performance index
	PQ	performance qualification

	PQR	product quality review
	PQS	pharmaceutical quality system
	QA	quality assurance
	QC	quality control
	QCL	quality control laboratory
	QRM	quality risk management
	RA	risk assessment
	RCA	root cause analysis
	SOP	standard operating procedure
	TAMC	total aerobic microbial count
	TFC	total fungi count
	TLC	thin layer chromatography
	URS	user requirements specifications
	UV	ultraviolet-visible spectrophotometer

Part 2	Brief summary of the findings and comments (where applicable)

Brief summary of the findings and comments

1. Pharmaceutical quality system

Production and control operations were specified in written form and GMP requirements were generally followed. Managerial responsibilities were specified in job-descriptions. Product and processes were monitored and the results taken into account at batch release; regular reviews of the quality of pharmaceutical products were conducted.

The Company had a defined structure and role of the quality systems. The QA functions were amongst:

- Managing documentation system and approval of the core documents,
- Approve or reject of intermediates, finished products (FPP),
- Review of BMRs,
- Preparation and approval of PQRs
- Review and approval of change controls,
- Review and approval of quality compliant investigations,
- Managing CAPAs
- Management of suppliers / contractors,
- Approval of quality specifications,
- BMR preparation
- Training
- Internal audits

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

2. Good manufacturing practices for pharmaceutical products

Manufacturing processes were defined and reviewed. Qualifications and validations were seen to be performed according to prepared protocols. Significant deviations from the initial protocol were recorded and investigated, root causes were determined and CAPAs were implemented where necessary. Systems were in place for handling complaints and recalling any batch of product from sale or supply.

Although, production in question was not running at the time of inspection, the site demonstrated the good manufacturing practices using another product on the same line.

The production was performed in a multi-product facility and production equipment were not dedicated. The overall design of sterile production facilities was found to be appropriate and well maintained. The preparation, filtration and filling operations were carried out in sequence as seen during the inspection.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

3. Sanitation and hygiene

The facilities and procedures for sanitation and hygiene established on the site were found to be adequate to ensure that premises and equipment were properly cleaned. All equipment inspected was in an appropriate condition. The gowning and changing procedures for entry into the manufacturing facilities were satisfactory and adequately described in SOPs (illustrated) which were displayed on the wall.

4. Qualification and validation

The Validation Master Plan was compiled and approved by the Corporate QA and formally adopted by the site. The VMP contained reference to the Corporate SOP on process validation. The site had local SOPs on process validation. The validation documents of Capreomycin injection were discussed.

According to the SOP aseptic process validation should be performed initially for any new or substantially changed process by performing 3 consecutive batches and on-going aseptic process validation should be performed every 6 months normally utilizing one batch.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

5. Complaints

The SOP on the management of drug product complaints was managed through TrackWise. The trending on complaints was done through TrackWise system. The procedure described timeline for handling critical and less critical complaints, it was however noted that two separate timelines were described for the US market and Rest of the World (ROW) for initial evaluation. In general, the procedure was found adequate which included investigation, root cause, classification of complaints, elevation of classification of complaints, CAPA, trending etc. The procedure was cross referenced to product recalls / market actions procedure. In 2016, two complaints

were received from Mylan Ireland for missing Batch No. on vial. These were found to be unconfirmed in the event that no sample or evidence was provided. In 2015, three complaints were received. Trending on complaints received in 2015 was done and found adequate.

6. Product recalls

Not inspected due to time constraints

7. Contract production, analysis and other activities

Not inspected due to time constraints.

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

Internal quality audit (self-inspection) procedure was reviewed. The site identified 6 quality systems, all these quality system were audited at least once/year. A separate procedure was in place for quality auditor certification program. Also a certified quality auditor list was available which identified the names of the 6 auditors (3 each lead and guest auditor), department, certified as lead/guest auditor, certified for (Quality System, Laboratory Control System, Production System, Packaging & Labelling System, Facility & Engineering System and Materials System) and certification validity. Although, all these auditors were selected from QA, there was no assurance if they will not audit their own department. From the audit record, it was confirmed that QA auditors had not audited their own department. Where required, the subject matter experts were used.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

9. Personnel

There appeared to be an adequate number of personnel qualified to perform and supervise the manufacturing and quality control. Controls were in place to prevent unauthorized people from entering production, storage and QC areas.

The personnel at the site were as follows.

Department	Strengths
Production	197
QA	54
QC (chemical and microbiology)	74
Engineering	43
Warehouse	17
HR and administration	06
Other support functions	10

There were no temporary workers employed in production areas.

10. Training

Training was provided in accordance with a written training programme.

Technical training procedure was reviewed. It was noted that technical induction training (GMP, GDP, and Data Integrity/DI) should be completed within 30 days of joining the organization. Upon successful completion of induction training, a certificate was given to staff. Personnel were not allowed to work unless they have completed training and certification. Training was also organized whenever SOP was revised (incident, complaint). The training team releases task in Documentum. The training procedure described preparation of quarterly and monthly training schedule for GMP, GDP and other types of training. The mandatory training was provided at least once every year. Quarterly training calendar classroom (January-March 2017), and on the job training (January-March 2017) schedule was available which confirmed topics covered on GMP, environmental monitoring program (EMP), data integrity (DI) etc. There was also a system to evaluate training after it was imparted to the staff i.e. practical and written. Written and on the job training assessment (practical evaluation) on Do's and Don'ts in aseptic area was reviewed for all 14 production personnel.

The personnel qualification by microbiological methods was available for the personnel.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

11. Personal hygiene

The level of hygiene observed and the measures taken to maintain the facility were considered acceptable. Hand washing, bathroom, and changing facilities were available in the first change room for each manufacturing area.

Basic uniforms for packing and laboratory consisted of overall, head cover, face mask and safety shoes were provided. Goggles were provided in laboratory. Uniforms in Grade A/B were sterile and consisted of overall, mask, hair cap, gloves, shoe covers, goggles.

12. Premises

Rest and refreshment rooms were separate from manufacturing and control areas.

Exposed surfaces were smooth, impervious and unbroken. Changing rooms were designed as airlocks and used to provide physical separation of the different stages of changing. Changing rooms were flushed with filtered air. Premises were cleaned and disinfected according to written procedures.

Sufficient space was given to avoid mix ups and cross-contamination. Storage space was provided for samples, reference standards, solvents, reagents and records.

The production premises were located on the ground floor of the building. The layouts of the facilities were available. The tour at the production focused on the Combi line-Lyo (3 compounding lines, filling line with lyophilization and capping). The environmental conditions (temperature, pressure, relative humidity) at the aseptic areas were continuously monitored, recorded electronically and printed out.

Assess to the controlled and in particular the aseptic areas were controlled by biometric identification. The basis of the authorization was the successful gowning validation and participation in media fill.

The aseptic and surrounding areas were supplied with AHUs (from 41 numbers, the aseptic areas were supplied by 12). The layouts showing controlled areas, pressure differences; AHUs were available and discussed.

There was a preventive maintenance (PM) program in place including all the critical equipment and the AHUs. The procedure for PM of AHU and forced draft ventilation was discussed.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

13. Equipment

Fixed pipework was labelled to indicate the contents and the direction of flow. Balances and other measuring equipment of an appropriate range and precision were available for production and control operations and were calibrated on a scheduled basis.

The number of lyophilizer installed in the Combi line-Lyo was 2. The SOP on the operation of lyophilizer provided instruction for vacuum leak test (VLT). The procedure was revised on 4 Nov 2016 based on WHO assessment comment and, test for VLT was added. The VLT was performed after cleaning in place (CIP) and sterilization in place (SIP) before starting lyophilization cycle.

The Qualification program of the critical equipment was defined in the VMP. The qualification records of the lyophilizer, and the steam sterilizer were discussed.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

14. Materials

Materials were received, sampled and tested according to the written procedures.

Materials were stored in the raw material, packaging material and finished product warehouses. The layout of the warehouses was available. The storage location together with the other data of the materials was available in the SAP. The codes identifying the raw materials, intermediates (semi-finished goods-SFG) and finished products (FPP) were available in the SAP system. The SAP records of the Capreomycin batches were discussed. Material management was supported by SAP system (including issuance of the batch numbers and generation of the analytical report and product release certificate) operated by the Corporate.

Raw materials were handled according to the procedure. The warehouse situated on the ground floor of the building with the following main facilities:

- Receiving bay
- De-dusting
- Quarantine areas (below 30°C as ambient, 20-25°C, 2-8°C) together with the rejected storage physically separated in cages at the ambient and 2-8°C parts.
- Approved areas (below 30°C as ambient, 20-25°C, 2-8°C).
- Sampling rooms for APIs and excipients
- Staging 1 and staging 2
- Dispensing 1 and Dispensing 2 (Grade D with a LAF of grade C)

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

15. Documentation

Documents were available and included SOPs, protocols and records. SOPs reviewed in the production areas were generally being followed and staff appeared appropriately knowledgeable as to their content.

The procedure described the main principles of the documentation system. The management of the SOPs (preparation, review, approval, etc.) was assured by the Document Compliance manager (DCM) software. The approved SOPs were automatically transferred to the “CARA” software which made it available for the concerned staff as “read only”. The obsoleted versions were made unavailable in the CARA automatically.

There was an SOP in place for preparation, issue, movement, retention and archive of Batch History Records. The general management of electronic data was defined in SOP. A corporate procedure on access control and password security management was available. The user groups, user privileges and the list of users of the Empower 3 system was available and discussed. The user levels were: Administrator, Site administrator, Reviewer, Analyst, Guest, Service engineer.

16. Good practices in production

In general production operations followed defined procedures. Deviations from procedures were recorded and investigated. Access to production premises was restricted to authorized personnel.

Process flow chart of Combi line-Lyo was shared with the inspectors. A blank BMR of Capreomycin (as sulfate) 1g powder for injection dated was reviewed. The compounding was done in manufacturing area 1 or 2 or 3 which has equipment of similar capacity. The batch size was 50L which can be compounded in any of these areas as noted from the batch record.

Secondary packaging rooms were spacious and lines well segregated.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

17. Good practices in quality control

The QC function was independent from other departments. Adequate resources were available to ensure that all the QC arrangements were carried out in a timely and ordered fashion. QC personnel had access to production areas for sampling and investigations as appropriate. The QC laboratory was responsible for testing raw materials, packaging materials, intermediates (semi-finished goods), finished products, water samples, stability samples and environmental monitoring samples.

There were two microbiology laboratories identified as analytical microbiology and environmental microbiology laboratory. These laboratories were located at two different locations serving the routine testing and environmental monitoring respectively. A general layout of microbiology laboratory was available and gowning procedure was found appropriate. The analytical microbiology tested non-sterile APIs i.e. microbial limit test, water including endotoxin, sterility for FPP and validation of methods, equipment and personnel. The sterility testing was performed under LAF (Grade A) with Grade B environment. The sterility room was equipped with three change rooms for personnel whereas sample was transferred through dynamic pass box. Three microbiologists were responsible for sterility testing. There was system in place for receiving, testing and storing of media, it was verified and found adequate. The laboratory was also equipped with double door autoclave, wherein unloading happens in Grade B environment.

The long term stability samples (normal and inverted) of the Capreomycin injection validation batches were available. The inventory of the stability samples was available in the LIMS software. The conditions (temperature and humidity) of the chambers were continuously recorded.

Retention sample storage was managed by the QC laboratory. According to the procedure, the samples of finished product (FP) batches where shelf life was important (commercial batches or validation batches to be commercialized) were retained. Besides FP samples, the raw materials of all the productions (including exhibit batches) were retained. The requirement of the room was below 25°C and the actual temperature was 22°C.

The issues related to this section have been adequately addressed by the manufacturer, and the same shall be verified during future inspections.

PART 3

Conclusion

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, **Mylan Laboratories Limited**, located at **Hosur Sterile Facility, Hosur, Tamil Nadu, India** was considered to be operating at an acceptable level of compliance with WHO good manufacturing Practices for pharmaceutical products.

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 2 years, provided that the outcome of any inspection conducted during this period is positive.

PART 4

List of GMP guidelines referenced in the inspection

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eight Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, 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.
<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-six Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, 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
http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1
5. WHO guidelines on good manufacturing practices for heating, ventilation and air-conditioning systems for non-sterile pharmaceutical dosage forms. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 5
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

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
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
<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
<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
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
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
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
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
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
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
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
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
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
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
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf
20. WHO Recommendations for quality requirements when plant – derived artemisin is used as a starting material in the prosecution of antimalarial active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 6
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf
21. WHO good manufacturing practices for biological products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 3
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex03.pdf
22. Guidance on good data and record management practices. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 5
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf

23. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf
24. WHO good manufacturing practices for biological products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 3
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex03.pdf