

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

Part 1	General information
Manufacturers details	
Company information	
Name of manufacturer	Hetero Labs Ltd.
Corporate address of manufacturer	Hetero Labs Ltd. Hetero Corporate, 7-2-A2, Industrial Estates, Sanath Nagar, Hyderabad – 500 018, Telangana, India
Inspected site	
Address of inspected manufacturing site if different from that given above	Hetero Labs Ltd. Unit-V Sy. No. Part of 439, 440, 441 & 458 TSIIC, Pharma SEZ, Polepally (village), Jadcherla (Mandal), Mahaboob Nagar (Dist.)- 509 301
Unit / block / workshop number	Unit-V (Block V and VA)
Manufacturing license number, (delete if not applicable)	50/MN/AP/2009/F/R (Unit-V) by Government of Telangana, India
Inspection details	
Dates of inspection	30 October to 03 November 2017
Type of inspection	Routine GMP inspection
Introduction	
Brief summary of the manufacturing activities	The Hetero Labs Unit V was located about 80 KM from Hyderabad city. There were three blocks (Block-V, Block-VA, and Block-VB) on the site with different multi-product formulation and packaging modules. Block V and Block VA were in the inspection scope. Cytotoxic products were manufactured in Block VB which was out of the scope of this inspection.
General information about the company and site	Hetero Labs Ltd, a division of Hetero group was established in 1993.

History	The site has been inspected by several regulatory authorities. The site has been inspected by WHO-PQT since year 2010. This was the fifth WHO-PQT, Geneva.
Brief report of inspection activities undertaken	
Scope and limitations	
Areas inspected	<p>Document reviewed including but not limited</p> <ul style="list-style-type: none"> • 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 • Validation and qualification • Data integrity • Sampling and testing of materials • Batch processing records • Materials management system <p>Site visited:</p> <ul style="list-style-type: none"> • Oral Solid Dosage (OSD) Production operations • Stability study QC laboratory and control system • Starting material and finished Goods warehouse
Restrictions	The tablet products manufactured on this site included the manufacture by dry, wet granulation and direct compression process. A number of the company's products were also manufactured using processes other than the products under WHO pre-qualification for which the wet granulation was employed. Neither of other two processes was inspected during this inspection.
Out of scope	Products not submitted to WHO for Prequalification
WHO product numbers covered by the inspection	<p><u>Prequalified products</u></p> <p>Efavirenz Tablets 600mg (HA399)</p> <p>Efavirenz/Emtricitabine/Tenofovir Tablets 600/200/300 mg (HA538)</p> <p>Lamivudine/Nevirapine/Zidovudine Tablets 150/200/300 mg (HA275)</p> <p>Lamivudine/Tenofovir Tablets 300mg/300mg (HA448)</p> <p>Lamivudine/Zidovudine Tablets 150mg/300mg (HA521)</p> <p>Linezolid Tables 600mg (TB299)</p> <p>Moxifloxacin Tablets 400mg (TB315)</p> <p>Efavirenz / Lamivudine / Tenofovir Disoproxil Fumarate Tablets 600mg/300mg/300mg (HA549)</p>

	<u>Products under assessment</u> Abacavir (as Sulfate) + Lamivudine 600mg/300mg (HA657) Sofosbuvir Tablets 400mg (HP002) Entecavir Tablets 0.5mg (HP005) Entecavir Tablets 1.0mg (HP006) Acyclovir Tablets 400mg (HA554) Valganciclovir (hydrochloride) Tablet, Film-coated 450mg (HA630)
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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

A system for quality assurance was established, with procedures covering key quality elements in place. The procedures were reviewed and discussed during the inspection. Operations were specified in written form and GMP requirements were essentially being met. Managerial responsibilities were appropriately specified in written job-descriptions. Product and processes were monitored and the results taken into account during batch release; regular monitoring and reviews of the quality of pharmaceutical products were being conducted according to documented schedules and procedures.

2. Good manufacturing practices for pharmaceutical products

Good manufacturing practices were implemented and followed. Required staff and system resources were provided. Manufacturing processes were clearly defined and documented. Qualification and validation were performed. Operators were trained to carry out procedures correctly, and comprehensive records were made during manufacture. Some minor deficiencies were noted.

3. Sanitation and hygiene

In general, premises and equipment were maintained at a satisfactory level of cleanliness. The company had a standard operating procedure as the basis for its approach to personal hygiene and sanitation in its production facility, with appropriate hand washing facilities.

Clean areas were cleaned frequently in accordance with approved written procedures. Environmental Monitoring of viable particles was regularly undertaken.

4. Qualification and validation

The company approach to validation was documented and explained in the Validation Mater Plan (VMP) and the VMP was briefly reviewed by the inspectors. The key elements of a qualification and validation programme were defined.

5. Complaints

Complaints were handled according to SOP Handling of Market Complaints and Quality Defects. SOP dealt both with quality (market and quality defects) and pharmacovigilance (ADR) complaints. Head QA or designee was responsible to receive complaints and responsible to start investigation. A template (complaint information form) was available to record information. The complaints were classified in critical (they need immediate recall), major or minor (they require 30 days to close investigation and take actions).

6. Product recalls

The SOP on Product Recall was reviewed. The head of QA was responsible for recall. The recalls were classified in class I (to be completed within 2 days from the communication); class II (to be completed within 7 days) and class III (to be completed within 15 days). Recall could be on voluntary basis and requested by Drug Authority. A mock recall was requested once a year at least for one batch in case not a recall was done.

7. Contract production, analysis and other activities

According to the Site Master File, there was use of external scientific, analytical or other technical assistance in relation to the products in the inspection scope. However, it was confirmed by the company that they have not been using external laboratories past one year.

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

The SOP on Self Inspection Programme was reviewed. QA was in charge to plan, organize self-inspection and monitor the CAPA implementation. Three types of self-inspections were performed: intra department (every sixth months), inter department (every sixth months) and Corporate QA (every sixth months). Additional self-audits could be performed following some unexpected events such as a recall, a complaint and a rejection.

9. Personnel

The manufacturer had an adequate number of personnel with the necessary qualifications and practical experience. 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.

10. Training

Training was not covered in detail by this inspection.

11. Personal hygiene

Changing and washing before entry to production areas followed a written procedure. Direct contact was avoided between the operator's hands and starting materials, primary packaging materials and intermediate or bulk product. No concerns of note were identified during the inspection. The approach to sanitation and hygiene was in general acceptable; during the inspection in the production areas, personnel wore adequate clothes related to the activities to be performed.

12. Premises

Generally premises were located, designed, constructed and maintained to suit the operations to be carried out. The layout and design of premises minimize the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination.

It was noted that daily differential pressure recording was lacking in traceability: the zero values, for HVAC supposed to be switched off, were not recorded and the recording time was not reported to cross reference when the HVAC was switched off.

Manufacturing areas were generally of a good standard and suitable for the activities conducted therein. Exposed surfaces were smooth, impervious and unbroken to minimize the shedding or accumulation of particles or microorganisms and permitted the repeated application of cleaning.

Block V was divided in 4 Modules, Module I included cleaning area and cleaned staging areas. All production modules were multi products and in Module II, IV and V was possible to manufacture different products at the same time into separate cubicles because each production room was equipped with separate airlocks for personnel and for materials maintained over pressure respect to the main corridor and production rooms.

Module III was single product because it was not equipped with airlock

The Block V included two sampling areas (respectively dedicated for active and excipients) and 4 dispensing booths (2 for excipients and 2 for actives). During the inspection one sampling area was operating and it was noted the correct behavior of the operators.

Block VA was divided into phase I and phase II and the phases were accessed through different change rooms from the main corridor. The facility had warehouse with unloading bay wherein incoming materials are received, de-dusted and check weighed. There were separate sections for storage of packaging material, API and excipients. Storage areas were of sufficient capacity. Receiving and dispatch bays were separated and protected materials and products from the weather. Segregation was provided for the storage of rejected, recalled, or returned materials or products. The materials were handled through the SAP system. Raw material warehouse, manufacturing and packaging activities were carried out on the ground floor and utilities were located on the first floor. The facility had 7 granulation suites, additional 3 blending suites, 6 compression areas, 5 coating areas and 7 packaging lines that were operational at the time of the inspection. Each manufacturing cubicle was accessed through personnel airlocks with interlocking doors and there was also separate material airlock for each manufacturing cubicle. Changing rooms were designed as airlocks with interlocking doors that provided physical separation of the different stages of gowning. Pictorial procedures were displayed and mirrors were in place.

The sampling and dispensary areas had the necessary reverse laminar airflow (RLAF) booths in Block V and VA. For Block VA, there was a separate dispensing booth for API and excipients. There was one sampling booth dedicated for APIs, dispensing booths for API and excipients. No operation was being carried and all the AHUs for the sampling and dispensing booths were switched off and no risk assessment had been performed for this activity.

QC laboratories were separated from production areas. Adequate space was provided for samples, reference standards, solvents, reagents and records.

13. Equipment

The equipment installed for tablet manufacturing was of a good standard. The facility and equipment appeared to be running well with no significant stoppages on either line noted during the inspection. The detailed procedures for the operation of key equipment were generally well documented.

It was noted that in some production steps, the product was not protected by environment conditions: bins receiving the tablets, hopper feeding the inspection machine, bottles after air-flushing before filling, hopper feeding bottles caps.

Laboratory equipment and instruments were suited to the testing procedures undertaken in general; however, the company has not considered to network the analysis instruments including HPLC, GC and IR.

Preventive maintenance procedures (PMP) were prepared for each production and utility equipment in accordance with the manufacturers' instructions. Annual PMP was performed in detail whereas bimonthly review was also performed. Based on the nature of the breakdown, PMP was updated. In addition, based on the comments made by the inspectors and consultants, additional checks were added in PMP. Breakdown history was maintained. In addition to the PMP, annual calibration program schedule was available. There was no formal review done on unplanned breakdowns for each equipment and utilities. It is recommended to prepare training modules on PMP and breakdowns.

14. Materials

Starting materials and packaging materials were purchased from approved suppliers. Printed packaging materials were stored in secure areas.

Material receipt was handled through SOP on receipt and storage of raw material (WH003, version 18) dated 31/08/2017 and provided for verification of consignments against the vendor list. It was noted that the material receipt procedure did not provide for raising of discrepancy noted on container weights and there was not set acceptance criteria for weight variation. The material storage area was monitored for temperature conditions from a hot spot established during temperature mapping studies. There was no alarm in place in the warehouse to alert in the event of any excursions.

Finished products were held in quarantine in production area until their final release, after which they were transferred to and stored under appropriate and monitored conditions in a separate store, in a different building across the road.

Rejected materials and products were marked as such and stored in designated secure areas.

The SOP on Vendor Qualification was reviewed. QA department is responsible to approve/qualify vendors. The process starts when the purchase department identified a new potential vendor. A questionnaire had to be send by QA/CA department to vendor and three samples of three batches were required for analysis. For raw materials, in case no three lots were available, the vendor could be provisionally qualified. Once three batches had been tested, the vendor was qualified and included in the qualified vendor list. A site inspection was required for API vendors; for excipients a site inspection was required only in some cases such as a DMF was not available, the vendor was located in no PIC/S-area, if some critical issues were found in the questionnaire. A similar process was in place to qualify the packaging materials vendors. A periodical evaluation of vendors was performed (every 3 years for API, 5 years for excipients and for packaging materials) via on site assessment or vendor qualification questionnaire.

15. Documentation

In general, documentation was designed, prepared, reviewed and distributed according to a documented procedure. Documents were regularly reviewed and kept up to date.

Approved, signed and dated testing procedures and specifications were available for starting and packaging materials and for finished products.

Batch manufacturing records (BMRs) were retained for each batch processed. Before any processing began, checks were made that the equipment and work stations were clear of previous products, documents, or materials, and that the equipment was clean and suitable for use. Checks were recorded as part of the BMR. Batch records were with each process stage requiring multiple pages. Master formula was saved in the System Applications Product (SAP) system and records were paper based.

A batch packaging record (BPR) was retained for each batch packaged. Before any packaging operation began, checks were made that the equipment and work station were clear of previous products, documents or materials, and that equipment was clean and suitable for use.

The sample of BMR and BPRs reviewed were generally satisfactory.

16. Good practices in production

A brief visit to production areas was undertaken. The premises were relatively new and in a good state. Areas briefly inspected included the dispensing areas, granulation 2 where production of WHO prequalified products was done, compression area, and coating suite. The areas were generally clean and well maintained. According to the layout, areas were classified as Grade D. Flow was not always unidirectional, and a common airlock was used for material and personnel entry and exit to areas. The production was in operation at the time of inspection.

Finished products were held in quarantine until their final release, and stored under conditions established by the manufacturer. Separate areas were provided for storage of rejected materials and products, if any.

Before packaging operations begun, steps were taken to ensure that the work area, packaging line, printing machine and other equipment were clean and free from any products, materials or documents used previously. The line clearance was performed and recorded in the BPRs.

17. Good practices in quality control

The QC function was independent of other departments. Adequate resources were available to ensure that the QC arrangements are effectively and reliably carried out in general.

There were four QC laboratories including chemical and microbiology QC laboratories. The lab for stability studies was briefly inspected. The stability testing specifications, testing data, standardization of working references were reviewed.

In general, the laboratory was found adequate, spacious and well equipped with modern equipment and instruments. The laboratory uses Caliber LIMS for the management of incoming materials, in-process samples and finished products. The data generated from the analysis were fed into LIMS and certificate of analysis was generated through LIMS. The different groups were responsible for the analysis of raw materials, packaging materials, in-process, cleaning validation samples and finished product samples. The testing of stability study was performed in Block V-A. the competency matrix for all analysts was available. The analytical worksheets were printed from the LIMS.

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, Hetero Labs Ltd. Unit-V, located at Sy. No. Part of 439, 440, 441 & 458 TSIIC, Pharma SEZ, Polepally (village), Jadcherla (Mandal), Mahaboob Nagar (Dist.)- 509 301 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 3 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