World Health Organization

20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

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

| **Part 1** | **General information** |
|---|---|
| **Manufacturers details** | |
| Company information | |
| Name of manufacturer | ***Cipla Ltd*** |
| Corporate address of manufacturer | Cipla Limited<br>Cipla House<br>Peninsula Business Park<br>Ganpatrao Kadam Marg<br>Lower Parel, Mumbai – 400 013<br>India<br>Telephone: 91 22 24826000<br>Facsimile : 91 22 24826120<br>24 hours contact Telephone No. : +91 832 2889000 / 2889199 / 2889101 |
| **Inspected site** | |
| Address of inspected manufacturing site if different from that given above | Plot No: L-139, S-103 & M-62,<br>Verna Industrial Estate, Salcette,<br>Goa 403722, India |
| Unit / block / workshop number | **Unit-III, IV and VII and PD-II** |
| Manufacturing license number, (delete if not applicable) | 536; 546; 831; (Unit III and IV)<br>611; 616; 830 (Unit VII and VII PD II) |
| **Inspection details** | |
| Dates of inspection | 13 to 17 June 2016 |
| Type of inspection | Routine GMP Inspection |
| **Introduction** | |
| Brief summary of the manufacturing activities | Manufacture, blending / granulation, compression, coating and packaging of solid unit dosage forms including tablets, and hard gelatine capsules, topical preparations (creams, gels and ointments. (Non-beta-lactam products only / non-beta-lactam and |

| | |
|---|---|
| | beta-lactam products / beta-lactam products /reproductive health products ) |
| General information about the company and site | Cipla Ltd is a public limited company. The company has several manufacturing sites in India with that at Goa being its largest complex. Other sites in India are located at:<br><br>• Bangalore - Pharmaceutical formulations and APIs<br>• Patalganga - Pharmaceutical formulations and APIs<br>• Kurkumbh - Pharmaceutical formulations and APIs<br>• Goa - Pharmaceutical formulations<br>• Baddi - Pharmaceutical formulations<br>• Sikkim - Pharmaceutical formulations<br>• Bommasandra - APIs<br>• Indore - Pharmaceutical formulations<br><br>The manufacturing site of Cipla Ltd, Plot No: L-139, S-103 & M-62 (hereafter referred to as Unit-III, IV, VII and VII-PD-2) is located in Verna Industrial Estate, Verna – Salcette - Goa and was inspected by a WHO prequalification inspection team on the above mentioned dates. |
| History | *The last WHO inspection to Unit III, IV and VII was held in November, 2013.* |
| **Brief report of inspection activities undertaken** | |
| **Scope and limitations** | |
| Areas inspected | Production and controls of Unit-III, IV, VII and PD-II |
| Restrictions | None |
| Out of scope | None |
| WHO product numbers covered by the inspection | **<u>Unit-III</u>**<br>HA039 Nevirapine Tablet 200mg<br>HA051 Zidovudine Tablet, Film-coated 300mg<br>HA057 Ciprofloxacin (hydrochloride) Tablet, Film-coated 250mg<br>HA056 Ciprofloxacin (hydrochloride) Tablet, Film-coated 100mg<br>HA059 Ciprofloxacin (hydrochloride) Tablet, Film-coated 750mg<br>HA060 Lamivudine/Zidovudine Tablet, Film-coated 150mg/300mg<br>HA353 Lamivudine Tablet, Film-coated 150mg<br>HA354 Lamivudine Tablet, Film-coated 300mg<br>HA365 Lamivudine/Nevirapine/Zidovudine Tablet, Film-coated 150mg/200mg/300mg<br>HA439 Emtricitabine/Tenofovir Disoproxil (fumarate) Tablet, Film-coated 200mg/300mg<br>HA500 Efavirenz/Emtricitabine/Tenofovir Disoproxil (fumarate) Tablet, Film-coated 600mg/200mg/300mg<br>TB227 Levofloxacin Tablet, Film-coated 500mg<br>TB205 Levofloxacin Tablet, Film-coated 250mg<br>Amodiaquine (hydrochloride) + Artesunate Amodiaquine (Hydrochloride) Tablet + |

Artesunate Tablet 153mg + 50mg
MA064 Artemether/Lumefantrine Tablet 20mg/120mg
HA058 Ciprofloxacin (hydrochloride) Tablet, Film-coated 500mg
HA352 Efavirenz Tablet, Film-coated 600mg
HA401 Tenofovir disoproxil (fumarate) Tablet, Film-coated

**Unit-IV**
HA039 Nevirapine Tablet 200mg
HA051 Zidovudine Tablet, Film-coated 300mg
HA052 Zidovudine Capsules, hard 100mg
HA056 Ciprofloxacin (hydrochloride) Tablet, Film-coated 100mg
HA057 Ciprofloxacin (hydrochloride) Tablet, Film-coated 250mg
HA058 Ciprofloxacin (hydrochloride) Tablet, Film-coated 500mg
HA059 Ciprofloxacin (hydrochloride) Tablet, Film-coated 750mg
HA060 Lamivudine/Zidovudine Tablet, Film-coated 150mg/300mg
HA352 Efavirenz Tablet, Film-coated 600mg
HA353 Lamivudine Tablet, Film-coated 150mg
HA354 Lamivudine Tablet, Film-coated 300mg
HA365 Lamivudine/Nevirapine/Zidovudine Tablet, Film-coated 150mg/200mg/300mg
HA401 Tenofovir Disoproxil (fumarate) Tablet, Film-coated 300mg
HA418 Emtricitabine Capsules, hard 200mg
HA438 Efavirenz Capsules, hard 200mg
HA439 Emtricitabine/Tenofovir Disoproxil (fumarate) Tablet, Film-coated 200mg/300mg
HA502 Lamivudine Tablet, Film-coated 30mg TB205 Levofloxacin Tablet, Film-coated 250mg
TB227 Levofloxacin Tablet, Film-coated 500mg
TB228 Cycloserine Capsules, hard 250mg
Amodiaquine (hydrochloride) + Artesunate Amodiaquine (Hydrochloride) Tablet + Artesunate Tablet 153mg + 50mg
MA064 Artemether/Lumefantrine Tablet 20mg/120mg
HA500 Efavirenz/Emtricitabine/Tenofovir Disoproxil (Fumarate) tablets, film-coated 6200/200/300 mg

**Unit-VII**
HA039 Nevirapine Tablet 200mg
HA051 Zidovudine Tablet, Film-coated 300mg HA052 Zidovudine Capsules, hard 100mg
HA056 Ciprofloxacin (hydrochloride) Tablet, Film-coated 100mg
HA057 Ciprofloxacin (hydrochloride) Tablet, Film-coated 250mg
HA058 Ciprofloxacin (hydrochloride) Tablet, Film-coated 500mg
HA059 Ciprofloxacin (hydrochloride) Tablet, Film-coated 750mg
HA060 Lamivudine/Zidovudine Tablet, Film-coated 150mg/300mg
HA353 Lamivudine Tablet, Film-coated 150mg HA365 Lamivudine/Nevirapine/Zidovudine Tablet, Film-coated 150mg/200mg/300mg

| | |
|---|---|
| | HA418 Emtricitabine Capsules, hard 200mg<br>HA438 Efavirenz Capsules, hard 200mg<br>HA439 Emtricitabine/Tenofovir Disoproxil (fumarate) Tablet, Film-coated 200mg/300mg<br>HA500 Efavirenz/Emtricitabine/Tenofovir Disoproxil (fumarate) Tablet, Film-coated 600mg/200mg/300mg<br>HA550 Atazanavir (sulfate) Capsules, hard 300mg (under assessment)<br>HA593 Efavirenz/Lamivudine/Tenofovir Disoproxil (fumarate) Tablet, Film-coated 600mg/300mg/300mg<br>HA608 Lopinavir/Ritonavir Capsules, hard 40mg/10mg (under assessment)<br>TB227 Levofloxacin Tablet, Film-coated 500mg<br>TB205 Levofloxacin Tablet, Film-coated 250mg<br>TB228 Cycloserine Capsules, hard 250mg<br>IN001 Oseltamivir (phosphate) Capsules, hard 75mg<br>Amodiaquine (hydrochloride) + Artesunate Amodiaquine (Hydrochloride) Tablet + Artesunate Tablet 153mg + 50mg<br>MA064 Artemether/Lumefantrine Tablet 20mg/120mg<br>IN012 Oseltamivir (phosphate) Capsules, hard 30mg<br>IN013 Oseltamivir (phosphate) Capsules, hard 45mg<br>HA354 Lamivudine Tablet, Film-coated<br>HA401 Tenofovir Disoproxil (fumarate) Tablet, Film-coated 300mg<br>HA352 Efavirenz Tablet, Film-coated 600 mg<br>HA518 Abacavir (as sulfate) + Lamivudine Dispersible tablets 60/ 30mg<br><br>**<u>Unit-VII PD-II</u>**<br>HA365 Lamivudine + Nevirapine + Zidovudine Film-coated tablets 150mg + 200mg + 300mg<br>HA489 Lamivudine + Tenofovir Disoproxil fumarate Tablets 300mg + 300mg<br>HA500 Efavirenz + Emtricitabine + Tenofovir Disoproxil fumarate Tablets 600mg + 200mg + 300mg<br>HA518 Abacavir (as sulfate) + Lamivudine Dispersible tablets 60mg + 30mg<br>Efavirenz/Lamivudine/Tenofovir Disoproxil (fumarate) Tablet, Film-coated 600mg/300mg/300mg |

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 well established with procedures for all key quality elements. In general the procedures reviewed were a good standard reflecting a good level of input from personnel with a good knowledge of WHO GMP requirements. Cipla had a well-established documentation infrastructure consisting of procedures, records, specifications and related documentation, approaches and policies to support quality management and quality assurance.

The actions taken or proposed to be implemented have been reviewed by the inspectors, and these were found to be acceptable. Their satisfactory implementation will be verified during future inspections.

**2. Good manufacturing practices for pharmaceutical products**

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

**3. Sanitation and hygiene**

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

Clean areas were cleaned frequently in accordance with an approved written programme. It was the practice to rotate the disinfectants used in the critical clean rooms. Monitoring of the microbial status of in use disinfectants was included in the environmental monitoring programme and was regularly undertaken.

Gowning for visitors and use of disinfectant was found satisfactory. Pest control was out-sourced to Pest Control (India) Pvt Ltd. Pest Control as well as Pest control records for June 2016 were reviewed.

**4. Qualification and validation**

The company identified what qualification and validation work was required. The key elements of a qualification and validation programme were defined. Documentary evidence was available that the premises, supporting utilities, equipment and processes were designed, installed, operated in accordance with their design specifications.

The reviewed validation master plan included description for the different types of validation in respect of process validation and the frequency of performing such processes. Further, the validation matrix for the formulation was reviewed and found adequate.

## 5. Complaints

The SOP for handling of complaints was a common procedure for all units and it was reviewed during the inspection of Unit-IX. There were no complaints received by the unit(s) for the HA365 and HA500 products as evidenced by documentary review.

## 6. Product recalls

The procedure on recall of products was applicable to all the units and was reviewed in the inspection of Unit-9. There were no recalls of products inspected in this unit. The SOP for recall of products was a common procedure for all units (site). It was reviewed in the inspection of Unit-9. There were no recalls for inspected products as evidenced by documentary review.

## 7. Contract production, analysis and other activities

This aspect was adequately covered in the inspection of Unit-9 and all matters were considered pertaining to all units in the site. Therefore, the inspection undertaken was deemed sufficient in this respect.

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

Not inspected due to time constraint.

## 9. Personnel

The manufacturer had an adequate number of personnel with the necessary qualification and practical experience. Responsible staff, specific duties were recorded in written job descriptions. Discussions with personnel reviewed that they were aware of the principles of GMP and received initial and continuing training, including hygiene instructions, relevant to their needs. Steps were taken to prevent unauthorized people from entering production, storage and QC areas through procedural measures and biometric access control system. An organization chart for the unit was available and its review that indicated the structure was appropriate.

## 10. Training

The SOP on training; a corporate procedure reviewed in the inspection of Unit-9 was found acceptable. The procedure on training in respect of contract workmen was not clear on how training was managed between Cipla Ltd and its associate company. For instance, in the case of Mr. Vijagan (Engineering Department) discussions revealed that there was another SOP by the associate company (SODEXO) on which personnel training was based on. He was an engineer assigned to perform duties on the service floor for utilities. Scope of the Cipla procedure covered this aspect of associated companies and yet there was no evidence of evaluation (induction training) as described in the procedure. There was no cross reference to the other

procedure in question. However, signed training reports were evaluated by the trainer though there were no comments made.

The actions taken or proposed to be implemented have been reviewed by the inspectors, and these were found to be acceptable. Their satisfactory implementation will be verified during future inspections.

**11. Personal hygiene**

The sanitation and hygiene measures in place at the time of the inspection were generally found to be adequate to assure the prevention of cross contamination/maintenance of cleanliness. Applicable procedures and pictorial instructions relating to sanitation and hygiene were available at the site of activities or workstation.

The level of hygiene observed was considered sufficient. All changing rooms were provided with documented and depicted procedures describing the gowning procedures. Mirrors were available to check on the gowning before entering in the production areas. There was also provision for hand sanitisation after gowning.

**12. Premises**

Generally premises were located, designed, constructed, adapted, and maintained to suit the operations being carried out. The design of premises was logical and laid out in a manner to minimize the risk of errors and cross-contamination and permit effective cleaning and maintenance. Premises were designed and constructed to facilitate good sanitation. The production area was laid out to allow production to take place in areas connected in a logical order corresponding to the sequence of the operations and to the requisite cleanliness levels.

Exposed surfaces were smooth, impervious and unbroken to minimize the shedding or accumulation of particles or microorganisms and permitted the repeated application of cleaning agents and disinfectants, where used. Changing rooms were flushed with filtered air. Changing rooms were designed as airlocks and used to provide physical separation of the different stages of changing. Changing rooms were equipped with mirrors. Airlock doors were interlocking (could not be opened simultaneously).

**Unit-III:** The ground floor for Unit-III included quality operations, raw material and packing materials warehouse; while the first floor: production, packaging and water utility section and technical area and the second floor, packaging, air handling unit and water system area.

**Unit-IV:** Adequate utilities were provided. The HVAC and purified water (PW) generation and distribution systems were inspected. AHU grouping and pressure differential monitoring layout No EP-044/F2/2 rev. 07 dated 10/06/16 was reviewed. AHU Grouping and Pressure differential layout rev. 13 dated 10/06/12 with drawing no U4/88/03 were reviewed showing layout for the first floor. Concerns were raised regarding the possibility of humidity increase from moisture that may arise from the paste preparation room in granulation 1 suit. The dedicated AHU, LACD-29 was inspected and it was noted that the AHU was synchronized with the BMS and any rise in humidity would be controlled automatically by the BMS. Any excursion would trigger an alarm.

In addition, the inspection covered premises of Unit-VII and PD-II and were found to be satisfactory.

## 13. Equipment

The equipment in the premises was maintained in a good state of repair and each piece of equipment had a unique identification number. Calibration and preventive maintenance stickers were placed on each critical equipment including balances and magnehelic gauges. They were found to be within the validity timelines for calibration and maintenance. Procedures were available for the cleaning of each piece of equipment in the production area and the activity was recorded. There were separate log books kept for the cleaning, usage and preventive maintenance of each equipment. The pipes for potable and purified water were well labelled and the direction of flow was also indicated.

A detailed floor layout of the building was presented. The clean area consisted of the production and quality control areas. The premises were well-maintained in all the places. Most fittings generally flushed with the walls and ceilings. All areas were clearly labelled as was all the pipe work with the contents and direction of flow.

The actions taken or proposed to be implemented have been reviewed by the inspectors, and these were found to be acceptable. Their satisfactory implementation will be verified during future inspections.

## 14. Materials

The plant used SAP for managing the materials. The SOPs for all the material handling processes were available. The materials were inspected upon receipt and relevant documentation was raised. The storage for quarantined and approved materials was not segregated as locations were assigned by the SAP and stock rotation was based on the principle of FEFO.

The environmental conditions were controlled and monitored. The temperature monitoring system included an audible alarm for out of limits of which it was challenged during routine preventive maintenance. There was adequate storage for all the materials in the warehouse. The receiving area was adequate and well covered to confer protection against the weather elements. The procedure for receipt of materials was reviewed and found adequate. It included the use of checklists and also provided for a comprehensive check for damages to the containers. An approved vendor list was available and was referred to during the receiving process for raw and packaging materials.

The actions taken or proposed to be implemented have been reviewed by the inspectors, and these were found to be acceptable. Their satisfactory implementation will be verified during future inspections.

## 15. Documentation

The units had relevant documentation to provide product traceability. The procedures were appropriately approved and placed at their respective work stations. All the processes of production and testing of materials and finished products as well as the parameters monitored were documented and the relevant records relating to product history were available. The information in the records was comparable to that in the Batch Manufacturing Record. All the equipment had status labels, the calibration details and numbered for ease of identification. Log books for the equipment were maintained.

Review in this area indicated that there was a robust documentation system in place both paper and electronic based.

The actions taken or proposed to be implemented have been reviewed by the inspectors, and these were found to be acceptable. Their satisfactory implementation will be verified during future inspections.

**16. Good practices in production**

The plant layout was unidirectional and there were separate entries for personnel and materials. Gowns with names of personnel for identification were provided for different areas of production. However, one colour code was used. Both written procedures and pictorial gowning instructions were available including IPA for sanitization at the respective areas. The production area maintained Class D grade and secondary packaging area were unclassified. The equipment bore status labels and was calibrated /verified.

The area was generally well maintained and clean. Biometric access control system upon exit from the corridors into the production cubicles and packaging areas were in place to control risk of cross contamination and contamination. The rooms had temperature, relative humidity and pressure monitoring equipment continuously using the validated Building Management System (BMS). The manufacturing processes were monitored and in-process control conducted at all stages.

The inspection covered production areas of Unit-III, IV, VII and PD-II and were found to be satisfactory.

The actions taken or proposed to be implemented have been reviewed by the inspectors, and these were found to be acceptable. Their satisfactory implementation will be verified during future inspections.

**17. Good practices in quality control**

The Quality Operations area was separate from the Production areas and had clearly dedicated areas for performing specific functions. In general, the environment was well cleaned, tidy and well maintained. Procedures for different operations/activities within the laboratory were within reach of personnel. Work performed by analysts in the laboratory was reviewed by QA laboratory reviewers. Stability testing carried out at common laboratory in QC-X building.

The actions taken or proposed to be implemented have been reviewed by the inspectors, and these were found to be acceptable. Their satisfactory implementation will 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, **M/s Cipla Ltd. Unit-III, IV, VII and VII-PD-2 Goa, India** at 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