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**
**of the FPP manufacturer**

| **Part 1** | **General information** |
|---|---|
| **Manufacturers details** | |
| Company information | |
| Name of manufacturer and address | PT. Kalbe Farma Tbk.<br>Delta Silicon Industrial Park<br>Jl. M. H. Thamrin Blok A3-1, Lippo Cikarang, Bekasi 17550, Indonesia.<br><br>PO. BOX 371, Bekasi 17037, Indonesia<br><br>Phone 62-21-89907333 (24 hours)<br>Fax 62-21-8972874<br>GPS Coordinate ; 6°19'15.4175" South, 107°7'0.1182" East |
| Corporate address of manufacturer | KALBE Building<br>Jl. Let.Jend. Suprapto Kav.4, Central Jakarta 10510<br><br>PO BOX 3105 JAK, Jakarta , Indonesia<br><br>Phone 62-21-42873888 – 89<br>*Fax 62-21-42873680* |
| **Inspected site** | |
| Address of inspected manufacturing site | As above |
| Unit / block / workshop number | Production line 8A |

| | |
|---|---|
| Manufacturing license number | • *CPOB Cairan oral non beta laktam (GMP non beta lactam oral liquid)*<br>Certificate Number: 4655/CPOB/A/XII/15<br>License Number: HK.07.IF/V/109/11<br>License Date: 18 May 2011<br>Valid until: 31 Dec 2020<br>• *CPOB Kapsul keras non beta laktam (GMP non beta lactam hard capsule)*<br>Certificate Number: 4654/CPOB/A/XII/15<br>License Number: HK.07.IF/V/109/11<br>License Date: 18 May 2011<br>Valid until: 31 Dec 2020<br>• *CPOB Semisolid non beta laktam (GMP non beta lactam Semisolid)*<br>Certificate Number: 4656/CPOB/A/XII/15<br>License Number: HK.07.IF/V/109/11<br>License Date: 18 May 2011<br>Valid until: 31 Dec 2020<br>• *CPOB Serbuk oral non beta laktam (GMP non beta lactam oral powder )*<br>Certificate Number: 4657/CPOB/A/XII/15<br>License Number: HK.07.IF/V/109/11<br>License Date: 18 May 2011<br>Valid until: 31 Dec 2020<br>• *CPOB Tablet biasa dan tablet salut non beta laktam (GMP non beta lactam tablet and coated tablet)*<br>Certificate Number: 4653/CPOB/A/XII/15<br>License Number: HK.07.IF/V/109/11<br>License Date: 18 May 2011<br>Valid until: 31 Dec 2020<br>• *CPOB Injeksi volume kecil non beta lactam (GMP non beta lactam small volume injection)*<br>Certificate Number: 5108/CPOB/A/I/18<br>License Number: HK.07.IF/V/109/11<br>License Date: 18 May 2011<br>Valid until: 07 Feb 2023 |
| **Inspection details** | |
| Dates of inspection | 24 – 28 May 2018 |
| Type of inspection | Initial inspection |
| **Introduction** | |
| Brief summary of the manufacturing activities | Manufacture including production, quality control and release of non-beta lactam:<br>• Tablet<br>• Coated tablet<br>• Capsule hard<br>• Oral Powder<br>• Ointments |

<table>
<tr><td></td><td>

- Suppositories
- Oral liquid
- Small volume parenteral
- Traditional medicines

</td></tr>
<tr><td>General information about the company and site</td><td>PT Kalbe Farma Tbk. ("Kalbe") was established on September 1966 in Tanjung Priok, North Jakarta. In July 1997, Kalbe moved to its current premises in Delta Silicon Industrial Park, Lippo Cikarang, Bekasi (“Cikarang Site”).<br><br>Products manufactured on the site consist of sterile products (small volume parenterals), non-sterile products (syrups, topical liquids, suspensions, emulsions, creams, gels, suppositories, ovule, tablets, film coated tablets, enteric coated tablets and hard capsules) as well as repack products (liquids, solids and semisolid dosage forms).</td></tr>
<tr><td>History of previous inspections by national medicines regulatory authorities</td><td>This was the first WHO inspection.<br>The site was inspected/audited by the following authorities:
<table>
<tr><th>Year of Inspection</th><th>Authority</th></tr>
<tr><td rowspan="2">2013</td><td>National Agency of Drug and Food Control (NADFC) Indonesia</td></tr>
<tr><td>Medical Technology & Supplies (CDDRA) Sri Lanka</td></tr>
<tr><td>2014</td><td>National Agency of Drug and Food Control (NADFC) Indonesia</td></tr>
<tr><td>2015</td><td>National Agency of Drug and Food Control (NADFC) Indonesia</td></tr>
<tr><td rowspan="2">2017</td><td>National Agency of Drug and Food Control (NADFC) Indonesia</td></tr>
<tr><td>NAFDAC (Nigeria)</td></tr>
</table></td></tr>
<tr><td colspan="2">Brief report of inspection activities undertaken</td></tr>
<tr><td colspan="2">Scope and limitations</td></tr>
<tr><td>Areas inspected</td><td>See Part 2 below</td></tr>
<tr><td>Restrictions</td><td>N/A</td></tr>
<tr><td>WHO product covered by the inspection</td><td>Anti TB</td></tr>
<tr><td>Abbreviations</td><td>
<table>
<tr><td>AHU</td><td>air handling unit</td></tr>
<tr><td>ALCOA</td><td>attributable, legible, contemporaneous, original and accurate</td></tr>
<tr><td>API</td><td>active pharmaceutical ingredient</td></tr>
<tr><td>APQR</td><td>annual product quality review</td></tr>
<tr><td>BDL</td><td>below detection limit</td></tr>
<tr><td>BMR</td><td>batch manufacturing record</td></tr>
<tr><td>BPR</td><td>batch packaging record</td></tr>
</table></td></tr>
</table>

| | |
|---|---|
| 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 |
| FG | finished goods |
| 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 |
| ID | identity |
| IR | infrared spectrophotometer |
| IPC | In process control |
| 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 |
| NIR | near-infrared spectroscopy |
| NMR | nuclear magnetic resonance spectroscopy |
| NRA | national regulatory agency |
| OQ | operational qualification |
| PHA | preliminary 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 |
| QMS | Quality management system |
| QRM | quality risk management |
| RA | risk assessment |
| RCA | root cause analysis |
| RH | relative humidity |
| RM | raw materials |
| RS | reference standard |
| SAP | system applications products for data processing |
| SFG | semi-finished goods |
| SOP | standard operating procedure |
| STP | standard test procedure |
| T | Temperature |
| TAMC | total aerobic microbial count |
| TFC | total fungal count |
| TLC | thin layer chromatography |
| TMC | total microbial count |
| URS | user requirements specifications |
| UV | ultraviolet-visible spectrophotometer |
| VMP | Validation Master Plan |
| WS | working standard |

| **Part 2** | **Brief summary of the findings and comments** |
|---|---|

## 1. Pharmaceutical quality system

*Principle*

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 in batch release; regular reviews of the quality of pharmaceutical products were conducted.

*Data integrity*

The SOP "Good documentation practice and data integrity guideline" was briefly discussed.

*Management review (MR)*

The SOP "Management review" was briefly discussed. Standard minimum agendas were specified. MR topics were presented as power point presentations. Presentation and meeting minutes were available.

*Quality risk management*

The SOP "Risk management (level two document – general document)" and SOP "Risk assessment and control management (level 3 documents)" were briefly discussed. The tools listed in the SOP were:

- FMEA
- HACCP
- FTA
- HAZOP
- PHA

According to the SOP performed RAs should be verified annually. A number of RAs were briefly discussed.

*Product Quality review*

The SOP "Product quality review" was briefly discussed. PQRs were prepared periodically according to the "moving" schedule.

For WHO submission only two pilot batches were manufactured, therefore PQR XX tablets was briefly discussed. This PQR covered batches manufactured from January 2017 – March 2018. According to the SOP HVAC, water and compressed air trends were recorded in separate reports.

The SOP "Statistical evaluation of PQR" was briefly discussed. Cpk was applied for assay, dissolution, individual weight and content uniformity. The SOP "Statistical data processing" was briefly discussed.

*Complaints and Product Recall*

The SOP "Customer complaint handling" was briefly discussed. Medical complaints were managed by a different SOP. QA Compliance department was responsible for complaint investigations. RPN was used for complaints classification:

- Very high
- High
- Medium
- Low

Complaints were trended annually.

Complaints registers 2017 and 2018 were presented to the inspectors. A number of complaint investigation reports were briefly discussed.

The SOP "Post marketing product handling" was briefly discussed. This SOP was related to counterfeit products.

The SOP "Product recall" was briefly discussed. Recalls were classified as:

- Class I, recall within 24 hours
- Class II, recall within 3 days
- Class III, recall within 7 days

Effectiveness of the SOP was evaluated by a mock recall once per year.

*Self-Inspection*
The SOP "Self-inspection" was briefly discussed. According to the SOP self-inspection should be carried out at least annually. Inspection schedule 2018 was presented to the inspectors. Non-conformities were classified as:

- Critical
- Major
- Minor

Inspection was carried out using department-wise check lists. A list of qualified auditors was presented to the inspectors.

*Supplier's qualification*
The SOP "Raw material and packaging materials supplier qualification" was briefly discussed. The list of approved suppliers was presented to the inspectors.

*Contracts*
Manufacturing activities related to XX product under prequalification process were not contracted out.

*Change controls*
The SOP "Change control" and its flow chart and matrix were briefly discussed. Changes were initiated by change requestor, approved by department head, submitted to the Site head, approved and then submitted to QA. This was initial review of change request. Final approval was done by responsible pharmacist QA.

A number of CCs were briefly discussed.

*Deviation management*
The SOP "Deviation handling" and SOP "Deviation and CAPA system" were briefly discussed. SOP was applicable for deviations that have impact on the quality, safety, efficacy of the product. RPN was used for deviations classification. A number of deviation investigation reports were briefly discussed.

*Documentation system*
Documents were available and included SOPs, protocols and records. SOPs in the production areas were generally being followed and staff appeared appropriately knowledgeable as to their content. A large number of documents, new and revised, had been approved in the weeks before the WHO inspection.

The following SOPs were briefly discussed:

- SOP "Handling of forms". Forms were issued by QA department and issuance recorded.
- SOP "Documents handling in QC laboratory". Analytical work sheets were issued by QC department
- SOP "Data management system". Batch related documents including analytical raw data were stored expiry date + 1 year. Validation documents were kept for product life cycle. Stability studies documents were stored until 2 years after product was delisted
- SOP "Retain samples and batch record". Retained samples were stored in a stand-alone retain sample building. FPPs retain samples were stored until expiry date + 1 year. APIs retain samples were stored for 6 years
- SOP "Release of products".

- SOP "Rework". In practice the repackaging of imported products with non-Indonesian packaging was the only form of rework done
- SOP "Returned goods". Register was available for 2018 returned products
- SOP "Batch numbering system"
- SOP "Release of finished goods". Batch processing records and analytical raw data including audit trail was reviewed by QA Responsible Pharmacist
- SOP "Creation of certificates of analysis". CoA was reviewed & approved by QC manager and Approved & Certified by QA Manager (Responsible Pharmacist).

Personnel

PT Kalbe Farma Tbk had a sufficient number of qualified personnel to carry out the tasks for which the manufacturer was responsible. PT Kalbe Farma Tbk had an adequate number of personnel with the necessary qualifications and practical experience.

The SOP "Personal hygiene" was briefly discussed. Eating, drinking, smoking, jewellery, cosmetics and personal medicines were not allowed in production and QC areas. Persons having an apparent illness or open lesions were not allowed to handle starting materials, packaging materials, in-process materials. Medical checks were carried out once per year.

*Key Personnel*

The Job description of Line Quality Assurance Manager was briefly discussed. Job descriptions were general for all four line Managers.

*Training*

The SOP "Training" and SOP "System of training KUA LIMA" were briefly discussed. KUA LIMA training module was developed on site. Training module was distributed to all employees.

The SOP "Competency assessment of level 4-5 (supervisors and managers)" was briefly discussed. Competency assessment was done according to the competency matrix. For competency assessment open questions were used. Re-assessment was performed every 3 years.

Training files and competency assessment files for Quality Assurance Manager and Internal Auditor were briefly discussed. Training and competency assessment files were maintained by HR.

The SOP "Competency assessment for level 1 – 3" was briefly discussed. Analyst's competency mapping and signature specimen lists were presented to the inspectors.

## 2. Production system

Production operations followed defined procedures in accordance with manufacturing and marketing authorizations. Deviations were approved in writing and investigated. Checks on yields and reconciliation of quantities were carried. Operations on different products were not carried out simultaneously or consecutively in the same room.

The logbook was spot checked for the XX in Line 8A. This was the equipment where final mixing took place and where the largest number of different product batches was in close follow-up. The logbook was well laid out; pages were numbered and reviewed by QA after each page, which in practice was almost daily. Cleaning activities and the time they occurred were recorded. Two types of cleaning were recorded, one before batch changeover and one before product changeover.

*Batch processing and packaging records*

The BMR was spot checked for XX tablets. The BMR layout was clear and entries were filled out legibly. Weighing was recorded using the system PAS-X by vendor Werum. Weights were also checked by a logistics supervisor. On weighing labels the identity of the logistic weigher could clearly be established. The weighing order was logical, with active substance being weighed last.

## 3. Facilities and equipment system

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. Access to the production premises was restricted to authorized persons. Change rooms doors were interlocked. The production areas and hallways were clean, spacious and well maintained. Gowning looked to be adequate to control contamination. Weighing rooms dedicated for Line 8A were briefly inspected. In granulation drying bags were used which were product dedicated. Sieves were checked before and after use. Metal detectors were used, 2 per compression machine. Challenge tests for metal detectors were recorded in logbooks. A set of challenge test devices were presented to the inspector.

A storage room was provided for storage of work in progress. Intermediate hold times were established. The humidity in the production and storage rooms in Line 8A was controlled (less than 40%RH).

The area for storage of retention samples was briefly inspected. The rooms were controlled for temperature and humidity.

Stability rooms were under R&D in a separate building on the site. All conditions were available. The room where the stability study at ambient conditions (≤30ºC and ≤75%RH) for XX tablets was performed was spot checked. The rooms were monitored by the system Wonderware and equipped with alarms.

*Validation Master Plan*

Validation Master Plan was briefly discussed. The SOP describing the creation of a Master Plan was also briefly discussed. The VMP covered all elements of validation, i.e. analytical methods, cleaning, processes, qualification of laboratory and production equipment and utility systems (HVAC, water, compressed air, pure steam, dust collection, gas, steam, electricity, facilities).

*Computerized systems validation*

Computerized system validation Master Plan was for 2018 was briefly discussed. There was an SOP on validation of all computerized systems, categorized as GAMP3 (Excel and PLCs), 4 (Oracle, PAS-X, LIMS, Empower 3 and DOC-MS).

*Production process validation*

SOP on Process Validation was briefly discussed as well as process validation of XX tablets. During validation holds times for intermediates were established. Studies were well executed and the report was very clear.

*Cleaning validation*

The SOP on Cleaning Validation was briefly discussed. The SOP described the procedure to select the worst case product for the validation study. The selection of worst case product was justified in an overview listing all current active substances on this Line. This was a well-designed study.

*Utilities*

*HVAC system*

AHUs were located in spacious rooms on the roof of the production building. The latest modification to the system was the installation of final filter units in 3 of the AHU installations that provided air to Class E rooms for Line 8A. The qualification data in report at rest were briefly discussed.

*Purified water system (PW)*

The PW system was spot checked. PW system was well maintained and all monitoring equipment, such as for TOC online, UV lamp working hours and conductivity was calibrated.

Laboratory premises

QC laboratories were separated from production areas. QC laboratories were designed to suit the operations to be carried out. Sufficient space was given to avoid mix ups and cross-contamination. Laboratory premises were spacious and had different rooms for instrumental analysis and chemical analysis.

The microbiological laboratory was separated from chemical/instrumental laboratory and had separate rooms for work with master strains and microbial limit test. Microbial limit test was performed in two LAFs. Work with master strains was done in a biosafety cabinet.

*Electronic data back - up*

SOPs on backup of laboratory instruments data were briefly discussed. SOP XX was applicable for instruments with Empower software, i.e. HPLC and GC, SOP YY was applicable for FTIR, UV and NIR.

*Access control and security policies for HPLC/GC computer systems*

The SOP “Analytical instruments security level system” was briefly discussed. There were six access levels to the HPLC & GC systems. SOP also specified four access levels to UV and NIR.

*Equipment calibration*
Laboratory equipment calibration and preventive maintenance schedules were presented to the inspectors. Cross checks confirmed that schedules were followed.
Analytical balances were verified daily according to the USP chapter 41. Calibration was performed twice per year. Standard weights & calibration certificate were presented to the inspectors.

Dissolution equipment was calibrated internally and externally twice per year (mechanical and chemical). HPLC and UV calibration was done externally annually.

*Preventive maintenance (PM)*
Laboratory equipment and instruments PM schedule for 2017 was presented to inspectors. Cross checks confirmed that schedules were followed.

Production equipment /utilities and facilities PM
PM schedules were based on information from the ERP system Oracle. Trending of maintenance data was done.

**4. Laboratory control system**
Laboratory equipment and instruments were suited to the testing procedures undertaken. Laboratory had adequate facilities, trained personnel and approved procedures for sampling, inspecting, and testing starting materials, packaging materials, and intermediate, bulk, and finished products, and for monitoring environmental conditions.

HPLCs and GC were connected to the network. UV, IR and NIR were stand-alone equipment, equipped with audit trails.

During inspection XX tablets 12 M stability analysis raw data were cross checked with instruments and standards usage log books.

*Good chromatographic practice*
The SOP “Good chromatographic practice in QC” was briefly discussed.

*Sampling procedures*
The SOP “Raw materials sampling” and SOP “Packaging materials sampling” were discussed. Bulk containers from which samples had been drawn were identified.

The SOP “Sampling plan establishment” was briefly discussed. Sampling of packaging materials was done according to the AQL sampling level II. Defects for foil used in XX packaging were specified as:
- Critical (AQL 0.010% )
- Major (AQL 2.5 %)
- Minor (4.0 %)

*Validation/verification of analytical procedures*
The SOP "Analytical method validation" was briefly discussed. This SOP was also used for verification of compendial methods.

*Reference standards*
The SOP "Handling of reference standards" was briefly discussed. This version of the SOP was effective from 30 April 2018. SOP described pharmacopoeia reference standards and working standards management. WS were dispensed in amber colour vials.

Contract testing
The company used the number of contract testing laboratories. For product under WHO prequalification contract laboratories were not used.

Out of specification
The SOP "OOS management" and its flow chart and SOP "Microbiological OOS handling" were briefly discussed. Procedure was based on MHRA guideline "Out of specification investigations".

Full OOS register (chemical and microbiological) 2017 and 2018 were presented to the inspectors. A number of OOSs were briefly discussed.

Environmental monitoring (EM)
EM trends Line 8A (grade E) for 2017 were presented to the inspectors.

Purified water (PW) monitoring
PW trends for 2017 were presented to the inspectors. Specification XX "Purified" water was spot checked.

## 5. Materials system

Handling of materials and products, such as receipt and cleaning, quarantine, sampling, storage, labelling, dispensing, processing, packaging and distribution was in accordance with written procedures and recorded.

The warehouses for raw materials, primary and secondary packaging materials, and finished products were inspected. Warehouse areas were temperature controlled. Sampling areas were present, and quarantine of products was both by physical segregation and computer status. For raw materials sampling was done on $\sqrt{n}+1$ container. Identity tests were done on every container.

T mapping study for raw material warehouse report No XX was briefly discussed.

## 6. Packaging and labelling system

The Batch Packaging Record was well laid out. Strip machine was used for XX tablets. The printing of batch data was checked by a supervisor. Strips were transported to the secondary packaging area.

**PART**
***Conclusion – inspection outcome***

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report **PT Kalbe Farma Tbk., located at Delta Silicon Industrial Park Jl. M. H. Thamrin Blok A3-1, Lippo Cikarang, Bekasi 17550, Indonesia** 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 report***

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2.
   ***Short name: WHO TRS No. 986, Annex 2***
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

2. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2.
   ***Short name: WHO TRS No. 957, Annex 2***
   http://www.who.int/medicines/publications/44threport/en/

3. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourth-sixth Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2
   ***Short name: WHO TRS No. 970, Annex 2***
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/

4. WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4
   ***Short name: WHO TRS No. 929, Annex 4***
   http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1

5. 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
   ***Short name: WHO TRS 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
   ***Short name: WHO TRS No. 937, Annex 4***
   http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf?ua=1

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

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

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

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

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

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

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

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

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

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

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

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

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

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
***Short name: WHO TRS 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. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 3
***Short name: WHO TRS 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. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 5
***Short name: WHO TRS 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. Fiftieth Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10
***Short name: WHO TRS No. 996, Annex 10***
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf