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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Active Pharmaceutical Ingredient Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	**Cipla Ltd.**
Corporate address of manufacturer	Cipla Ltd. Cipla House, Peninsula Business Park, Ganpatrao Kadam Marg, Lower Parel, Mumbai – 400 013, India
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Cipla Ltd, Plot D-7, Plot D-22, Plot D-27 M.I.D.C Industrial Area, Kurkumbh Village, Taluka-Daund, District-Pune, Maharashtra, 413 802, India D-U-N-S number of the site 917066446
Synthetic unit /Block/ Workshop	Unit-I (D-7) Unit-II (D-27) and Unit-III (D-22)
Inspection details	
Dates of inspection	8-12 April 2019
Type of inspection	Special GMP inspection
Introduction	
Brief description of the manufacturing activities	There were five manufacturing blocks for APIs at Unit-I (Plot D-7), two blocks for APIs at Unit-II (Plot D-27) and four blocks for APIs at Unit-III (Plot D-22). Dedicated manufacturing block were available for Hormone API's at Unit-III and Corticosteroid API's at Unit-I.
General information about the company and site	Cipla Ltd is a public limited company established in 1935 and managed by a Board of Directors. Cipla manufactures and markets a wide range of pharmaceutical formulations, Active Pharmaceutical Ingredients (API's) and medical device products.
History	The Corporate headquarters including corporate QA was located at Mumbai. Senior personnel were available there for providing support to the manufacturing units in the areas of technology, integrated product development, manufacturing, quality control, quality assurance, and regulatory affairs. Import-export and distribution activities were monitored from corporate QA.

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	The inspection involved spot checks of the quality assurance system and investigations focused on the operations relating to the manufacture, quality control and quality assurance of the 15 APIs that are under the WHO PQ, manufactured by Cipla Kurkumbh in Unit I, Unit II and Unit III. In addition, the WHO inspection performed an evaluation of the potential impact of the USFDA inspection (11-20 March 2019) and observations as listed in the USA Form 483 on the WHO Prequalified API's.
Restrictions	None
Out of scope	The APIs out of the scope of the WHO PQ were not covered
WHO APIs covered by the inspection	1. APIMF001 (Lamivudine) 2. APIMF007 (Nevirapine) 3. APIMF025 (Tenofovir Disoproxil Fumarate) 4. APIMF061 (Emtricitabine) 5. APIMF073 (Oseltamivir Phosphate) 6. APIMF075 (Lumefantrine) 7. APIMF154 (Nevirapine Hemihydrate) 8. APIMF189 (Atazanavir monosulphate) 9. APIMF199 (Abacavir Sulfate) 10. APIMF251 (Darunavir Ethanolate) 11. APIMF253 (Efavirenz) 12. APIMF295 (Sofosbuvir) 13. APIMF304 (Dolutegravir Sodium) 14. APIMF313 (Atazanavir monosulphate/Methanol route) 15. APIMF336 (Albendazole/under assessment)
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CIP	Cleaning in place
CoA	Certificate of analysis
CpK	Process capability
DQ	Design qualification
EDI	Electronic deionization
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis

GMP	Good manufacturing practices
HEPA	High efficiency particulate air
HPLC	High performance liquid chromatography (or high performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
IQ	Installation qualification
KF	Karl Fisher
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
MR	Management review
NC	Non conformity
NRA	National regulatory agency
OQ	Operational qualification
PHA	Process hazard analysis
PLC	Programmable logic controller
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
RO	Reverse osmosis
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer

Part 2	Summary of the findings and comments

1. Quality management

The quality management system (QMS) of Cipla is centrally (corporate level) driven but managed at sites to harmonize systems. A formal documented system of quality assurance was established, with procedures covering all expected key quality elements being in place. The QA and QC departments were independent of technical (production) operations. Operations were specified in the written form. Procedures were in place for notifying responsible management of regulatory inspections, serious GMP deficiencies, product defects, and related actions. The procedures that were reviewed and discussed during the inspection were generally satisfactory. Product and processes were monitored, and these results considered during batch release. Regular monitoring and reviews of the quality of APIs were being conducted according to documented schedules and procedures.

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

- TrackWise: implemented on 6th July 2017, used for deviations, complaints (log from CQA) and CAPA (related to non-conformance);
- Cipdox: used for SOPs, specifications and change controls;
- LIMS): Quality Control data management and printing of certificates of analysis. Full connectivity with pH meters, analytical balances, tap density; and functionality for OOS for the creation of OOS number and intimation through SAP, but rest of laboratory operations handled manually;
- SAP: used for material inventory management system tracking, generation of master BMR and BPR and vendor management. Initiation of retesting was through SAP and then handled through LIMS.

Annual Product Quality Review (APQR)

The APQR which was applicable to drug products, intermediates, and drug substances was reviewed. The review was performed based on the date of approval of the product as well as by distributing APIs/products into 12 months. The batches are trended using Minitab software wherein a minimum of 15 batches are required for trend analysis. If the batches manufactured in a year are less than 15, batches manufactured in the previous year would be considered to make a total of 15. The company calculates the Process Performance Index (Ppk).

Quality risk management (QRM)

Risk management by failure mode, effects and criticality analysis/FMECA was reviewed. The procedure was applicable to different aspects of pharmaceutical quality like development, manufacturing, testing, distribution, inspection and submission processes throughout the life cycle of drug substance, drug products including equipment, facilities, system, raw material, solvents, packaging, labelling, and manufacturing operations. The FMECA methodically breaks down the analysis of complex processes into manageable steps and risk priority number (RPN) was used to calculate risk. The RPN category was part of the procedure wherein 76 to less than 125, RPN is critical, 51 to 75 is major and so on. The procedure stated that FMECA are reviewed once every three months until all RPN are reduced to an acceptable level. Flow chart and FMECA log was part of the procedure.

Root cause analysis

Investigation and root cause analysis (RCA) was reviewed. The procedure described various investigation tools & techniques for conducting an investigation of non-conformance to identify the root cause or most probable cause that enables the determination of corrective actions and preventive actions. The procedure provided various tools such as fishbone diagram, 5-WHYs, fault tree analysis, brainstorming, a checklist for investigation and human error detection checklist. The RCA was handled manually, and data generated from the investigation cum RCA analysis were uploaded onto the TrackWise under CAPA module. The effectiveness check was verified through the TrackWise system.

Quality Management Review

Quality management review (QMR) requirements were outlined in the Quality Manual. The QMR procedure was described in the SOP "Quality Management Review". Management reviews were used to identify appropriate actions for continual improvement of the pharmaceutical quality system, e.g. improvement to manufacturing processes and products and allocation or re-allocation of resources and/or personnel training.

Deviation management

The SOP for "Deviation Handling" seen. Scope included deviations observed during any stage of receipt, handling drug substance and its storage, dispensing, processing, testing, manufacturing, packaging operations, transportation, systems, software operations, facility, validation, qualification, calibrations, maintenance and documentation involved in the drug product, drug substance & its intermediates.

Deviations categorised as planned, unplanned, and repetitive i.e. repetitive 3 times in the past 12months review period, or product shelf life, or record retention/scheduled revalidation/verification period. Also categorised as critical, major, or minor deviations. Root cause analysis described in SOP "*Investigation and Root cause analysis"*, included fishbone (cause and effect analysis) diagram technique, Fault tree analysis, 5-Whys analysis. The handling, root cause analysis, and approval of deviations that were reviewed by the inspection team appeared to have been properly done with respect to the SOP for deviation handling.

The issues noted from this section have already been addressed and will be verified during future inspections.

2. Personnel

High level requirements for training were provided in the Quality Manual for induction and on-the-job training. Training needs identification and refresher training considerations provided in the annual training schedules. Training evaluation by questionnaires, oral and written examinations. Retraining needs identified based on the performance evaluation, detailed observation of work performance, periodic audits/internal audits, deviations, market complaints, OOS & OOT.

The training procedure applies to all Cipla employees and all contract workmen, maintenance and to other service providers assigned to the GMP facility or working on GMP systems, including computer systems.

The issues noted from this section have already been addressed and will be verified during future inspections.

3. Buildings and facilities

Not inspected.

4. Process equipment

Not inspected.

5. Documentation and records

The Quality Manual was reviewed. It applied to all CIPLA units. Among other information, it lists the 6 sub-quality systems namely:

- Quality system,
- Production system,
- Facilities and equipment system,
- Laboratory control system
- Materials system, and
- Packaging and labelling system.

The Corporate SOPs were listed department-wise, site-specific SOPs and list of policy documents were available.

The details of the documents and records reviewed refer to each specific section in this report.

6. Materials management

Qualification reports for Sofosbuvir (two starting materials); Dolutegravir Sodium (three starting materials); Albendazole (one starting material) Tenofovir Disoproxil Fumarate (one starting material); Abacavir (two starting materials) were reviewed. Names of the manufacturers and location addresses were monitored in SAP system. Re-assessment report of the manufacturer team was reviewed. Re-assessment was done every three years.

The SOP for selection, evaluation and approval of manufacturer of API starting material/intermediate was comprehensive, beginning from identification of the new manufacturer, receive filled questionnaire, and three batch samples, CoA, and other documents, and analyse samples, conduct audit and approve or reject.

Audit schedule for manufacturer/supplier of API, API intermediates, excipients, and packaging materials was available. Audits are not required to be done for manufacturers of starting materials that are used by the manufacture to produce intermediate materials.

The issues noted from this section have already been addressed and will be verified during future inspections.

7. Production and in-process controls

Selected batch manufacturing records were reviewed alongside the corresponding current process validation reports with respect to the Validation SOP "Process validation in API Manufacturing".

Critical parameters identified and monitored e.g. impurity profile at the crude stage and various crystallization steps, drying process, micronisation, etc. determining the attributes like chemical purity, impurity profile, physical characteristics such as particle size, bulk and tapped density, polymorphic forms, moisture and solvent content, homogeneity, and others. Monitor drying temp range, micronisation pressure range.

The process outlined as charging of raw materials, reaction (validated), filtration, drying (validated), Milling (validated), blending (validated), sifting and packing. Process validation of Albendazole, and Tenofovir Disoproxil Fumarate were reviewed and found adequate.

8. Packaging and identification labelling of APIs and intermediates

Not inspected.

9. Storage and distribution

Not inspected.

10. Laboratory controls

Laboratory non-conformance investigation procedure was reviewed. The procedure describes the process for handling out of specification, out of trend, laboratory incidents, and laboratory obvious error. This corporate procedure was applicable to APIs, FPPs and intermediates produced by Cipla. The investigation was performed in a phased manner. It appeared that the OOS process flow diagram was not very clear regarding retesting and resampling activities including hypothesis testing.

Quarterly trend analysis of OOS for Unit-I, II and III were reviewed.

The issues noted from this section have already been addressed and will be verified during future inspections.

11. Validation

Cleaning validation

Cipla's Kurkumbh API manufacturing site manufacture more than 100 APIs in three units. Most of these APIs are manufacture using shared facility including equipment, utilities, etc. The corporate SOP on cleaning validation for APIs was reviewed. It was noted that separate cleaning validation procedures were in place for APIs and FPPs. The draft procedure incorporated the EMA requirement of permitted daily exposure (PDE) to calculate the Maximum Allowable Carryover (MACO) in addition to standard therapeutic daily dose (TDD) and a general limit of 10ppm. Based on the calculation using TDD, 10ppm, and PDE, whichever is less will be taken as MACO limit. The PDE assessment of 3 WHO PQ APIs (Atazanavir Sulfate, Darunavir Ethanolate, and Emtricitabine) had been performed by the company's in-house toxicologist. The rest of the PQ APIs as well as for other APIs, it was indicated by the company that PDE was being performed. The issues noted from this section have already been addressed and will be verified during future inspections.

Analytical method validation

Details of method validation/method transfer & commercialization of WHO APIs was obtained. From the summary document, it was noted that all the tests/characteristics were validated before the commercialization of the prequalified APIs.

The determination of elemental impurities by ICP-MS was introduced based on the recent requirement. The SOP for the determination of elemental impurities in drug substance/excipients was reviewed. The procedure was drafted in accordance with the ICH Q3D requirement. It was noted that the determination of elemental impurities had been performed for most of the prequalified APIs and initiated based on the risk analysis performed by the QA.

The issues noted from this section have already been addressed and will be verified during future inspections.

12. Change control

Reviewed change control SOP, provided a procedure for the system of how changes are proposed, assessed, documented approved and implemented and to provide traceability of changes regarding the document, system, facility, instrument, equipment, product lifecycle, others. Scope included all changes (addition, revision, deletion, transfer related to the product, documented system, facility, equipment, instrument, system change (includes software change), and others. Other changes that were encountered included changes in vendors.

Changes were classified as major, moderate and minor depending on whether the change would have a direct impact or not, on the quality, purity, potency, strength, stability, safety, efficacy, or physical characteristics of the product or drug substance. The SOP had electronic signatures. Review of electronic change control data showed that a total of 850 change requests made for all the three API Units.

13. Rejection and re-use of materials

Not inspected.

14. Complaints and recalls

Complaints

SOP "Handling of product complaints", applies to all APIs Units and to the Formulation unit. Scope drug substance and drug products manufactured for the local market as well as for the export market. Complaints managed in TrackWise software. Classified as critical (potentially life-threatening or could result is a serious health risk with serious medical consequences) and non-critical (could cause illness or mistreatment) complaints and categorised as technical complaints (related to quality parameters of the product) or medical (related to adverse event or reaction) complaints.

Timelines for preliminary response to the complainant was provided as 15days for noncritical complaints; and one day for critical complaints. SOP provides for trend analysis and flow chart. Complaints first review 30 days, second review 45days and close-out within 60days of login.

Product recalls

Recall SOP "Recall Procedure for API" was reviewed. No actual recall was made in the last three years for the API side. Recall procedure simulation done by dummy recalls. The most recent was done on 06/09/2018. The SOP requires simulation done once in two years.

The SOP "Corrective action and preventive action" was reviewed and noted that CAPA were monitored in TrackWise software. Scope of CAPA is all CAPA arising out of OOS, OOT, OOAC ("out-of-action limit or "out-of-action alert limit" for used), audit findings, deviations, product complaints, recalls, analytical incidence in laboratory, rejection, annual product quality review, quality management review, risk assessment and change in regulatory/pharmacopoeial requirements, and other sources of quality data.

The issues noted from this section have already been addressed and will be verified during future inspections.

15. Contract manufacturers (including laboratories)

Selection, evaluation, and approval of contract testing laboratory were reviewed. The procedure delineated how contract testing laboratories were selected, evaluated and approved. For the release testing including testing of the stability samples of all WHO APIs, Cipla's on-site laboratory is capable to perform all tests and therefore does not send samples to contract testing laboratory. Method validation for some of the WHO prequalified APIs was performed by Sitec, Mumbai.

Quality technical agreement between Cipla and Sitec dated 23rd May 2017 was available. The agreement defined the roles and responsibilities of the contract giver and acceptor.

The issues noted from this section have already been addressed and will be verified during future inspections.

Part 3	Conclusion – Inspection outcome

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, ***Cipla Ltd (Unit I, II, III)***, located at ***Plot D-22, Plot D-27, Plot D-7, MIDC Industrial Area, Kurkumbh Village, Taluka-Daund, Pune District, Maharashtra, India*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines for APIs.

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 active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2. ***Short name: WHO GMP for APIs or WHO TRS No. 957, Annex 2***
   http://apps.who.int/medicinedocs/documents/s20119en/s20119en.pdf

2. 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 GMP*** or ***WHO TRS No. 986, Annex 2***
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

3. WHO good manufacturing practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourth-Sixth Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2.
   Short name: WHO TRS No. 970, Annex 2
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/
4. WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-Ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4.
   Short name: WHO TRS No. 929, Annex 4
   http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1

5. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8. ***Short name: WHO HVAC Guidelines*** *or* ***WHO TRS No. 1010, Annex 8***
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_1010/en/

6. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4.
   Short name: WHO TRS No. 937, Annex 4
   http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf?ua=1

7. WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1.
   Short name: WHO 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 production 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. 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 GDRMP guidance or WHO TRS No. 996, Annex 5
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf

22. 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 Multisource guidance or WHO TRS No. 996, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

23. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 10.
Short name: WHO TRS No. 1010, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf