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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
of the FPP manufacturer

Part 1	**General Information**
Manufacturer's Details	
Company information	
Name of manufacturer	**PT. SANBE FARMA Penicillin Plant** Jalan Mahar Martanegara. No 162 (Jl. Leuwigajah No. 162) RT.01, RW.12, Kelurahan Baros, Kecamatan Cimahi Tengah, Kota Cimahi - Indonesia Telephone number : +62 226613311 Fax number : +62 226613297 Latitude : -6,900524 Longitude : 107,546979
Corporate address of manufacturer	PT. SANBE FARMA Jl. Taman Sari No. 10 Bandung 40116 Indonesia Telephone number +62 22420 7725 Fax number +62 22423 8476
Inspected site	
Address of inspected manufacturing site if different from that given above	As above
Unit / block / workshop number	Unit II Penicillin Plant production 2nd floor, secondary packaging 1st floor
Manufacturing license number	Manufacturing licence from National Agency for Drug and Food Control (BPOM/NADFC), Republic of Indonesia: Licence no.: HK.02.06.IF/V/264/2015 Date of issue: 22 June 2015 Valid until: Permanent
Inspection details	
Dates of inspection	20-21 February 2017
Type of inspection	Routine
Introduction	
Brief summary of the manufacturing activities	Manufacture of Oral Solid Dosage Forms (Tablets and Capsules). Manufacture of Oral solid Powders for suspension for oral use. The site inspected was dedicated to the manufacture of penicillin formulations.

<table>
<tr><td></td><td>There were two physically separated departments: one for penicillin compounds and one for both cephalosporins and carbopenems compounds.</td></tr>
<tr><td>General information about the company and site</td><td>PT Sanbe Farma is an Indonesian pharmaceutical based group of companies who conducts formulation development, manufacturing and marketing of medicines, primarily for domestic sale in Indonesia.

PT SANBE FARMA head office is located in Bandung, West Java, Indonesia.

PT SANBE FARMA Penicillin Plant Unit II is located in Cimahi, Bandung, Indonesia, and is the facility dedicated to production of penicillin products and cephalosporin products in the PT Sanbe Farma group. The factory is situated at Jalan Mahar Martanegara. No 162 (Jl. Leuwigajah No. 162) RT.01, RW.12, Kelurahan Baros, Kecamatan Cimahi Tengah, Kota Cimahi - Indonesia, 10 km from Bandung City in Eastern area.

The manufacturing building is located on 5,000 square meters of land with one manufacturing block and ancillary areas. The site is involved in the manufacture of penicillin and cephalosporin products; oral solid dosage forms (capsules, tablets), powders for oral suspension and dry syrup, and sterile dry powder for injection.</td></tr>
<tr><td>History</td><td>The site was inspected by WHO in November 2014.
The site has been inspected by the following national authorities:

<table>
<tr><th>DATE</th><th>AUTHORITIES</th></tr>
<tr><td>25 - 26 June 2014</td><td>NAFDAC, Nigeria</td></tr>
<tr><td>2 - 3 March 2015</td><td>Pharmacy and Poisons Board, Kenya</td></tr>
<tr><td>22 – 26 May 2015</td><td>National Drug Authority, Uganda</td></tr>
<tr><td>29 – 31 July 2015</td><td>National Agency for Drug and Food Control of Republic of Indonesia (Badan POM RI /NADFC RI)</td></tr>
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Good Manufacturing Practices Certificates:

Certificate No.: 4392 / CPOB / A / IV / 15
Issued by: Badan POM RI /NADFC RI
Dosage form: Tablet and Coated Tablet of Penicillin and its Derivatives
Date of issue: April 29, 2015
Valid until: Jun 27, 2018

Certificate No.: 4393 / CPOB / A / IV / 15
Issued by: Badan POM RI /NADFC RI
Dosage form: Hard Capsule of Penicillin and its Derivatives
Date of issue: April 29, 2015
Valid until: Jun 27, 2018

Certificate No.: 4394 / CPOB / A /IV / 15
Issued by: Badan POM RI /NADFC RI
Dosage form: Oral Powder of Penicillin and its Derivatives</td></tr>
</table>

	Date of issue: April 29, 2015 Valid until: Jun 27, 2018 Certificate No.: 4395 / CPOB / A / IV / 15 Issued by: Badan POM RI /NADFC RI Dosage form: Sterile Powder for Injection of Penicillin and its Derivatives Date of issue: April 29, 2015 Valid until: Jun 27, 2018
Brief report of inspection activities undertaken	
Scope and limitations	
Areas inspected	See Part 2 below
Restrictions	N/A
Out of scope	Penicillin dry powders for syrup, sterile penicillin powders for solution for injection, cephalosporin and carbopenem Facility and Microbiological laboratory
Product covered by the inspection	Amoxicillin 250mg Dispersible Tablets for United Nations Commission on Life Saving Commodities (Amoxsan® 250). Amoxsan® 250 was manufactured on contract basis for its corporate but legally independent and authorized sister company PT Caprifarmindo Laboratories.

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
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

Brief summary of the findings and comments

1. Pharmaceutical quality system (PQS)

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.

Quality Risk Management

The SOP "Risk management" was reviewed. Risk assessment (RA) was categorized as:

- Periodic RA
- Non – periodic RA

Risk assessment was divided in:

- Risk identification
- Risk analysis
- Risk evaluation
- Risk control
- Risk acceptance
- Risk communication
- Risk review

Failure modes and effects analysis (FMEA) was used as the basis for most risk assessment performed to date.

Product Quality Review (PQR)

The SOP "Product quality review" was reviewed. The timeline for finishing the PQR was one month after compiling data for related product. A PQR work schedule was presented to the inspectors. This schedule should be reviewed so as to smooth the work cycle for PQRs and allow for more prompt completion of the report after the end of the review period.

Process capability was calculated using Cpk.

The document PQR Amoxan® 250 dispersible tablet was presented to inspectors. PQR covered batches made from January 2015 – December 2015.

Management review (MR)

The SOP "Management review" was reviewed. According to the SOP scheduled MR review shall be arranged by each department performed quarterly. Non-scheduled MR review was conducted if there were findings which highly impact product quality or manufacturer.

The SOP was applicable, but not limited to:

- Follow-up action's from pervious reviews
- Process performance and product conformity
- CAPAs
- Customer feedback and complaints

- Internal quality audits
- Changes and quality system planning
- Recommendations for improvements
- External assessments such as regulatory inspections and customer audits

Deviations

The SOP "Deviation report" and its flow chart were reviewed. The SOP was applicable to unplanned deviations. Deviations and their target close out were classified on the basis of risk priority numbers. Formal tools including Ishikawa diagram and 5 Why's were used for root cause analysis.

Deviation report logbooks were maintained month wise by QA. Deviations were trended yearly and trends for 2016 were presented to the inspectors.

Corrective actions and preventive action

The SOP "Corrective actions and preventive actions" and related CAPA No XX were reviewed. CAPAs were proposed by manager or supervisor of each department. QA manager was responsible for reviewing and approving CAPAs. According to the SOP trending of CAPAs should be done annually.

Change control (CC)

The SOP "Change management" and flow chart were discussed. SOP was applicable for any GMP related changes.

Deviation report logbooks were available and maintained month-wise by QA. Deviations were trended yearly and trends for 2016 were presented to the inspectors. CCs were trended annually.

2. Good manufacturing practices for pharmaceutical products

Manufacturing processes were defined and reviewed. Qualifications and validations were being performed and documented. Significant deviations were recorded and investigated, root causes were determined and CAPAs were implemented. Systems were in place for handling complaints and recalling any batch of product from sale or supply.

3. Sanitation and hygiene

The company had an SOP as the basis for its approach to personal hygiene and sanitation in its production facilities. Microbial monitoring was performed.

In general, premises and equipment were maintained at a satisfactory level of hygiene and maintenance. The facility though rather old of design and fabric was nevertheless being operated with a very high cleanliness.

4. Qualification and validation

The company had identified what qualification and validation work was required and this was described in its Validation Master Plan (VMP) which contained all the key elements of a qualification and validation programme. The VMP was generally satisfactory and complete. Documentary evidence was available that the equipment and processes have been designed, installed, operated in accordance with their design specifications.

The inspectors were told that hold time studies had been performed for:
- Dispensed raw materials
- Blended products
- Core tablets

Due to the time constraints hold time studies protocol/report were not reviewed.

5. Complaints

The SOP "Product complaint handling" was reviewed. Complaints were classified regarding product quality:
- Class I (minor)
- Class II (major)
- Class III (critical)

and
- Adverse reaction

Complaints registers for 2015 and 2016 were presented to the inspectors. Complaints were trended yearly.

6. Product recalls

The SOP "Product recall" was discussed. Recalls were classified as per BPOM/ NAFDC guidelines:
- Grade I - recall within 24 hours
- Grade II – recall within 5 days
- Grade III – recall within 7 days

Recall effectiveness was evaluated by mock recall. If there was not a real recall, it required that a mock recall should be performed every 2 years.

The QA manager was responsible for dealing with recalls. The Head of Quality had overall responsibility for dealing with recalls.

7. Contract production, analysis and other activities

Amoxsan® 250 was manufactured on contract basis for its corporate but legally independent and authorized sister company PT Caprifarmindo Laboratories.

A third party toll manufacturing agreement between PT Caprifarmindo Laboratories (CAPRI) and PT Sanbe Farma (SANBE) No XX was reviewed.

Quality agreement between CAPRI and SANBE No XX was available and discussed.

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

The SOP "Audit" was discussed. Inspection was carried out by a self-inspection team, using check lists. An inspection report was written by the team and CAPAs addressed by the inspected department.

Observations were classified as:
- Critical
- Major
- Minor

The companies audit check list had the following headings:
- Quality management and personnel
- Standard operations procedures
- Self-inspection
- Premises and equipment
- Warehousing areas

9. Personnel

There was an adequate number of personnel qualified to perform and supervise the current level of manufacturing and its quality control. Steps were taken to prevent unauthorized people from entering production, storage and QC areas.

Separate groups of dedicated personnel, including engineering personnel work in penicillins and cephalosporins/carbopenems departments. There was SOP rules in place for managers to whom the supervisory level staff report restricting them from visiting both the penicillin and cephalosporin zones on the same working day.

Number of employees:

Department	
Penicillins	
Production	81
Packaging	51
Cephalosporins/carbopenems	
Production	69
Packaging	47
Quality Assurance	12
Quality Control penicillins	30
Quality Control Cephalosporin	34
Validation	8
Document Control Officer	2
Production Planning and Inventory Control	39
Engineering	34
Personnel & GA	37
EHS	5
Total	449

10. Training

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

11. Personal hygiene

Direct contact between the operator's hands and starting materials, primary packaging materials and intermediate or bulk products were avoided. Smoking, eating, drinking, chewing, and keeping plants, food, drink, smoking material and personal medicines prohibited in production, laboratory and storage areas.

12. Premises

The facility was relatively unusual as the same building housed both the penicillin and cephalosporin/carbopenem products although the building was zoned to isolate the various production floors and technical zones. Each zone had segregated access controls for materials and personnel and appeared to effectively separated. HVAC was completely separated and had exhausts on opposite sides of the building to reduce risks of cross contamination.

Inspectors were informed by BPOM RI/NADFC RI inspector that soon PT Sanbe Farma will be formally ordered to completely separate penicillin's and cephalosporin's/carbopenems production buildings. It was confirmed by the site that construction had already commenced on a new site for cephalosporin's and carbopenems, each in different buildings on the new site. This new site is approximately 1 km from the current facility and should be complete and fully operational in 3 years. After this time the existing site will be dedicated to penicillin's only with refurbishment of the older facilities also planned.

Ancillary areas

Rest and refreshment rooms were separate from manufacturing and control areas and separated between two production departments.

Production areas

Penicillin products were manufactured and primary packed on 2nd floor, secondary packaging was carried out on 1st floor.

Production premises were approximately 20 years old and appeared to be nearing the end of the useful working life. Nevertheless the production areas were adequately maintained and the inspectors consider that they remain suitable up to the planned decommissioning and upgrade after the re-location of cephalosporin's to the new factory in 3 years' time. Should there be any delays in the refurbishment/relocation plans the inspectors should be informed.

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. Entry and exit to the production corridor was via air shower. Staff were also required to shower on exit of the facility at the end of the working shift. Premises were cleaned and disinfected according to written procedures.

Quality control areas

Sufficient space was available to allow orderly work flows in the lab and avoid mix ups and cross-contamination. Storage space was provided for samples, reference standards, solvents, reagents and records.

There were separate quality control and microbiology laboratories for penicillin's located within each block from those for cephalosporin/carbopenems testing.

13. Equipment

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

The purified water generation system was the same for penicillin and cephalosporin's/carbopenems departments. Penicillin and cephalosporin/carbopenem departments had separate PW storage tanks and distribution loops. The water room was only very briefly viewed but appeared orderly and well maintained.

14. Materials

Materials were received, sampled and tested according to the written procedures.
Penicillin starting materials were received in separate warehouse and transported by dedicated lift to the second floor.

Packaging materials were received in the warehouse located in separate location. On site there were separate satellite packaging materials storage room.

15. Documentation

Documents were available and included SOPs, protocols and records. SOPs were generally followed with no major violations noted during the inspection.

The SOP "Release and reject of finished product" was reviewed. The QA manager was responsible for releasing or rejecting routine finished products, validation batches and deviation batches. Amoxsan® 250 quality control tests were performed at PT Sanbe Farma Unit II, but released by CAPRI QA.

The SOP "Product rework" and SOP "Returned product handling" were discussed.

16. Good practices in production

Production operations followed defined documented procedures. Deviations from procedures were recorded and investigated. Access to production premises was restricted to authorized personnel. In general the inspectors considered that the number of deviations reported in a year was somewhat low compared to the number of batches manufactured and recommended that the company QA audits the reporting of deviations robustly to verify if there is under reporting of deviations into the QMS.

17. Good practices in quality control

General

The QC function was independent from other departments. Adequate resources were available to ensure that all the QC arrangements were carried out. QC personnel had access to production areas for sampling and investigations as was appropriate.

All test equipment (HPLCs, GCs, IRs and UVs) were standalone instruments. HPLCs had LC systems 1.25 software on their respective workstation PCs.

The SOP "Audit trail in HPLC" was reviewed. There were three access levels specified.

The SOP "Data integrity" was reviewed. According to the SOP audit trails and meta-data was reviewed before batch release. The matter of archiving of test records including e-records was discussed as were the ALCOA (attributable, legible (permanent), contemporaneous, original and accurate) principles for good documentation and data management practices. Issues were noted concerning the locking of clocks on computer work stations. Analysis was performed on one of three standalone instruments. The desirability of moving to a lab networked based system was discussed.

Out of specification results (OOS)

The SOP "Investigation of OOS" was reviewed. This was applicable for investigation of OOS results of starting materials, packaging materials, intermediate bulk products and finished products obtained in QC and microbiology laboratory as well as in stability studies.

OOS registers were different for chemical and microbiological labs. Registers were month wise.

Monitoring of PW

The SOP "Water quality monitoring" was reviewed. Microbial analysis of samples from return loop and all user points was analysed every week.

PW results were trended annually. Monthly reports were available. PW trends for 2016 were discussed. The data reviewed were satisfactory.

The SOP "Starting material sampling" was reviewed. For identity verification all API and excipients containers were sampled and ID tests performed.

Reference materials

The corporate SOP "Reference standard and working standard" was reviewed during Sanbe Unit III inspection. Working standards were prepared and dispensed by R&D department.

Amoxicillin reference materials were stored in refrigerator at 2-8 ºC. T in the refrigerator was continuously recorded using data loggers; data was uploaded and checked daily. Refrigerator was equipped with local alarm system. It was advised to connect the alarm system to the company security as it was the situation for the stability chambers alarm system.

Stability studies

Stability chamber temperature and RH sensors were connected to the software and recorded continuously. T was monitored every day and the printed data were collected once per week. Chambers were equipped with a local sound alarm, and remotely connected to the company site security post.

Retention samples

Finished product and APIs retention samples were stored 15–25 ºC. T in the room was continuously recorded on charts. Charts were reviewed once per week.

Storage period for finished product was expiry date + 1 year and for APIs was 2 years after finished product release.

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, PT. SANBE FARMA Penicillin Plant, located at Jalan Mahar Martanegara. No 162 (Jl. Leuwigajah No. 162) RT.01, RW.12, Kelurahan Baros, Kecamatan Cimahi Tengah, Kota Cimahi – Indonesia was considered to be operating at an acceptable level of compliance with WHO good manufacturing practices for pharmaceutical products.

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 used for assessing compliance

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/
   Short name: WHO TRS No. 986, Annex 2

2. 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

3. 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/

4. 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
Short name: WHO TRS No. 970, Annex 2
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/

5. 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

6. 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

7. 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

8. WHO Good Practices for Pharmaceutical 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/

9. 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/

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. Fifties 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. Fifties 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. Fifties 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