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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. SANBE FARMA Sterile Preparations Plant** Jl. Industri Cimareme No.8, Desa Cimareme, Kecamatan Ngamprah, Kabupaten Bandung Barat – 40553, Indonesia. Building A Telephone number +62 22 686 7966 Fax number +62 22 686 7969 North latitude: - 6,865159 East longitude : 107,494871
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	Unit III
Block	A
Manufacturing license number	Manufacturing license from National Agency for Drug and Food Control (NADFC) , Republic of Indonesia: License no.: HK.07.IF/V/402/14 Date of issue: 26 September 2014 Valid until: Permanent
Inspection details	
Dates of inspection	13-14 February 2017 and 16-17 February 2017
Type of inspection	Routine
Introduction	
Brief summary of	PT. SANBE FARMA Sterile Preparations Plant , manufactures and controls sterile

the manufacturing activities	products in the following dosage forms: Small and large volume parenterals including infusions: liquid injections, dry powders for injection, eye drops, ear drops, eye ointments, and fat emulsions The company produces no highly toxic or hazardous products in Unit III Building A. Oxytocin is the most potent of the materials handled. The site includes a separate and dedicated building for the handling of high potency for the handling of cytotoxic drugs.
General information about the company and site	PT SANBE FARMA, Unit III, located in Cimareme, Padalarang, Bandung - Indonesia, is the facility dedicated to production of non-beta-lactam injectable products within the PT Sanbe Farma group. The factory is situated Jl. Industri Cimareme No.8, Desa Cimareme, Kecamatan Ngamprah, Kabupaten Bandung Barat – 40553, Indonesia. Building A. The site complex adjoins property operated by a sister company, PT Caprifarmindo. Laboratotries. The PT Sanbe Unit III Building A site was involved in the manufacture of Small Volume Parenterals (SVPs) and Large Volume Parenterals (LVPs – these are mainly in Poly Propylene plastic bags) products. The site houses separate areas for SVPs and LVPs. In the SVP area there were separate facilities for aseptically prepared formulations and aseptic filling into ampoules and vials as well as separate plastic eye drop lines. The company also has extensive facilities in Unit III for LVP terminally sterilized products, dry injection and fat emulation dedicatedly. To the rear of Unit III there were two separate and dedicated buildings. One of these was dedicated to the manufacture of cytotoxic drugs and the other biological products. Each had its own management, facilities and services as well as laboratories. In addition, there was an additional site dedicated to beta-lactam products located 10 kilometers from Unit III, for oral solid dosage forms (OSDs) and injectables. This site is located at Unit II, Jalan Mahar Martanegara. No 162 (Jl. Leuwigajah No. 162) RT.01, RW.12, Kelurahan Baros, Kecamatan Cimahi Tengah, Kota Cimahi - Indonesia. The inspection of the beta-lactam facility is reported separately.
Brief report of inspection activities undertaken	
Scope and limitations	
Areas inspected	See Part 2 below
Restrictions	Only Corima ampoule line was inspected
Out of scope	• LVP terminally sterilized (TS) products. • SVP terminally sterilized (TS) products (there was a second ampoule line used

	for TS ampoules). • SVP aseptic powder filling. • Aseptic eye drop manufacture.
WHO product numbers covered by the inspection	RH050 Oxytocin Solution for injection 10 IU/mL
Abbreviations	

AHU	air handling unit
ALCOA	attributable, legible, contemporaneous, original and accurate
AQL	Acceptance quality limit
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
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
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
TOC	Total organic carbon
URS	user requirements specifications
UV	ultraviolet-visible spectrophotometer
VMP	Validation Master Plan
WFI	water for injection
WS	working standard

Part 2	Brief summary of the findings and comments (where applicable)

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

Quality Risk Management

The SOP was reviewed. Risk assessment followed the standard approaches described in ICH Q9 met the general requirements of WHO GMP norms and standards:

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

Failure modes and effects analysis (FMEA) was used for risk assessment, and the company's main approach to risk assessment was to follow a unified system based upon FMEA. The SOP gave little attention to other risk assessment tools which might be more appropriate under certain circumstances.

In the FMEA approach scores from 1- 4 was used for individual elements of the Risk Priority Number (RPN) calculation.

Risk registers were prepared month wise.

RA XX "Risk assessment for YY injection" was discussed. This was generally satisfactory at the high level but did lack sufficient detail and granularity in others.

Product Quality Review (PQR)

The SOP "Product quality review" was reviewed. The PQR schedule for 2016 and 2017 was presented to the inspectors.

A single common PQR was prepared for all Oxytocin (and other) market variant products made according to the same base manufacturing process.

Statistical tools were used for data presentation and analysis. Process capability was calculated using Cpk.

PQR for Santocyn® injection (Oxytocin Solution for injection 10 IU/mL) was reviewed:

The PQR was broadly comprehensive and acceptable covering most of the requirements of WHO GMP.

Management review (MR)

The SOP "Management review" was reviewed. According to the SOP quality system review shall be performed quarterly. The SOP was applicable, but not limited to:

- Follow-up action's from previous 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 flow chart were reviewed. The SOP was applicable to unplanned deviations. Deviations and their target close out, were classified with the system based on risk assessment.

Ishikawa diagrams were used for root cause analysis.

Corrective actions and preventive action

The company has a unified CAPA SOP which was used to handle most CAPA arising from several reporting mechanisms. CAPAs related to the self-inspection were presented separately and were linked to the specific self-inspection.

The SOP "Corrective actions and preventive actions" was inspected together with the log and specific examples chosen by the inspectors. CAPAs were proposed by manager or supervisor of each department and the QA manager was responsible for reviewing and approving CAPAs prior to their implementation. CAPAs registers were produced month wise.

Change control (CC)

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

CC registers were maintained by QA.

2. Good manufacturing practices for pharmaceutical products

Manufacturing processes were defined and reviewed. Qualifications and validations were seen to be performed according to prepared protocols. Significant deviations from the initial protocol were recorded and investigated, root causes were determined and CAPAs were implemented where necessary. 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 of clean room personnel was performed as part of routine batch control.

Generally, the facilities were noted to be clean and well organized during the inspection.

4. Qualification and validation

Aseptic process validation

The SOP "Aseptic process validation" and "Aseptic process validation protocol /report (Media fill run) VAL-XX and VAL-YY were reviewed.

According to the SOP aseptic process validation should be performed initially for any new or substantially changed process by performing 3 consecutive batches and on-going aseptic process validation should be performed every 6 months normally utilising one batch. For sequential media fills the use of the largest ampoule size and smallest ampoule size were rotated every 6 months.

The most recent media fill was reviewed. The numbers of ampoules were filled with non-sterile Tryptic Soy Broth – TSB media. It was noted that the normal Oxytocin injection filling time was 12 hours. Media simulation was done in 6 phases, totally 18 hours.

According to the SOP section X prior to incubation the containers should be inverted or otherwise manipulated so as to ensure that all surfaces are thoroughly wetted by the growth media. During media fills ampoules were inverted every day and the records of this procedure presented to the inspectors.

The document "Justification to define mimic process of ampoule line products for aseptic process validation (Media fill run)" was discussed. This was generally satisfied and the inspectors were satisfied that the media simulation was sufficiently representative of routine production.

Autoclave validation

The new autoclave adjoining the aseptic ampoule line for garments and spare parts sterilization was installed in October 2015. IQ&OP protocol/reports were available. Autoclave re-qualification protocol VAL-XX and report VAL-YY were discussed. The Bowie Dick test was performed once per day for the garments load.

Depyrogenation oven qualification

Depyrogenation oven IQ&OQ was finished 18 January 2016. IQ&OQ protocol (VAL-XX & VAL-YY) and report were spot checked. Hot air oven qualification report VAL-ZZ was also spot checked.

Clean room qualification

The air to the ampoule filing room was supplied by the AHU XX. Performance qualification report VAL-XX after changes "at rest" was reviewed. The following tests were carried out:

- Air changes per hour/air velocity
- Air flow pattern
- Pressure differentials
- T and RH

- Facility cleaning verification
- Microbial counts
- Particulate counts
- Particulate removal tests

HVAC system was equipped with alarms, which were said to be routinely challenged.

Temperature mapping
The SOP "Temperature and humidity mapping of controlled storage area" was spot checked.

Temperature mapping protocol "Pre-mapping temperature and relative humidity protocol" VAL-XX and report "Pre-mapping temperature and relative humidity protocol" VAL-YY were reviewed.
Leak test validation
Oxytocin was filled into 2 mL glass ampoules. Validation of the leak test had been performed in autoclave by vacuum. Validation report VAL-XX "Autoclave X for leak test" was reviewed and discussed.

5. Complaints
The SOP "Product complaint handling" was discussed. Complaints were classified regarding product quality:
- Class I
- Class II
- Class III

and
- Adverse reactions

Complaints register for Unit III 2015 and 2016 was presented to the inspectors. Month-wise registers were used.

Several complaints investigation documents were reviewed.

Complaints were trended yearly.

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

The QA manager was responsible for dealing with recalls. The head of quality had overall responsibility for dealing with recalls.

Recall effectiveness was periodically evaluated by mock recall. If there was not real recall, mock recall should be performed every 2 years.

7. Contract production, analysis and other activities

Manufacturing operations and laboratory testing relating to oxytocin were not contracted out. Pest control activities and irradiation of eye drop bottles and components were contracted out.

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

The SOP "Audit" was discussed. Inspection was carried out by a nominated self-inspection team.

Inspection was carried out using check lists. Inspection report was written by the team and CAPAs addressed by the inspected department.
Observations were classified as:

- Critical
- Major
- Minor

Check list had the following headings:

- Quality management and personnel
- Standard operations procedures
- Self-inspection
- Premises and equipment
- Warehousing areas
- Dispensary
- Parenteral operations and eye drops
- Sterilization of parenteral and eye drops (Sterilization by filtration)
- Finishing of sterile products
- Quality assurance / quality control department

Suppliers' audits and approval:

The SOP "Vendor approval of new supplier for raw material" was discussed. There was only one supplier of Oxytocin API.

9. Personnel

There appeared to be an adequate number of personnel qualified to perform and supervise the manufacturing and quality control. Controls were in place to prevent unauthorized people from entering production, storage and QC areas.

Number of employees:

LVP	419
Production	163
Packaging	256
SVP	206
Production	99
Packaging	107
Quality Assurance	17
IPC	35
Quality Control	97
Validation	20
DCC	3
PPIC	76
Engineering	66
IT	22
Personnel and GA	41
Others	44
Cost Accounting	6
Security	20
Driver	18
Total	**1046**

The SOP "Personnel qualification for manual visual inspection" was reviewed. Oxytocin ampoules visual inspection was performed manually. Operators were re-qualified once a year.

10. Training

Training was provided in accordance with a written training programme.

The SOP "Training" was reviewed. There were the following training modes in place:

- General orientation
- On the job training
- SOP training
- Outside training and seminars

Training effectiveness was evaluated by verbal questions, open questions and written answers.

The SOP "Personnel hygiene application and aseptic technique in sterile products manufacturing" was discussed. The SOP "Personnel qualification working in aseptic area" was also discussed.

Personal files for Mr. XX, a filling operator and Mr. YY, from maintenance engineering in Sterile Preparation Plant were spot checked.

The SOP "Preparation of specimen for qualification manual visual inspection" was spot checked.

11. Personal hygiene

All personnel, prior to and during employment, had to undergo an initial health examination. Thereafter regular health examinations were carried out every year. Personnel conducting visual inspections had to undergo periodic eye examinations every six months. Direct contact between the operator's hands and starting materials, primary packaging materials and intermediate or bulk products was avoided. Smoking, eating, drinking, chewing, and keeping plants, food, drink; smoking material and personal medicines was prohibited in production, laboratory and storage areas.

12. Premises

Ancillary areas

Rest and refreshment rooms were separate from manufacturing and control areas.

Production areas

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. Premises were cleaned and disinfected according to written procedures.

Quality control areas

Sufficient space was given to avoid mix ups and cross-contamination. Storage space was provided for samples, reference standards, solvents, reagents and records.

13. Equipment

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

14. Materials

Materials were received, sampled and tested according to the written procedures.

15. Documentation

Documents were available and included SOPs, protocols and records. SOPs reviewed in the production areas were generally being followed and staff appeared appropriately knowledgeable as to their content.

16. Good practices in production

In general production operations followed defined procedures. Deviations from procedures were recorded and investigated. Access to production premises was restricted to authorized personnel.

Oxytocin injection was manufactured on a XX ampoule line. This was the only line used by the company for aseptic filing of aseptically manufactured ampoules. The company had two other lines for terminally sterilized ampoules; however these were not within the scope of inspection.

Since the previous inspection, the company had installed a Fedegari hot air oven between the grade C and grade B filling room. This was now in routine use for the sterilisation and depyrogenisation of ampoules for aseptic filing and represented significant improvement to the aseptic process over the situation that was seen previously.

The aseptic ampoule filling line was used to fill approximately 20 different products. Oxytocin was the most potent of those products. The solution transfer line hoses and silicone tubing between the filling needles, filing pumps and balancing tank on the machine were stated to be dedicated to a specific active ingredient and were re-used. Other parts of the filling machine were made from stainless steel and was multipurpose use e.g. filing pumps. Cleaning had been validated on a matrix basis.

Secondary packaging rooms were spacious and lines well segregated.

The SOP "Visual inspection manually for sterile product" was spot checked.

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 in a timely and ordered fashion. QC personnel had access to production areas for sampling and investigations as appropriate.

All test equipments (HPLCs, GCs, IRs and UVs) were standalone instruments.

HPLC No X was routinely used for Oxytocin analysis and was checked during the inspection.

The SOP "Audit trail in HPLC which use LC solution system" was spot checked. There were three access levels specified.

The SOP "Preparing and reviewing QC analytical report" was discussed.

The SOP "Sampling for analysis of starting material" was spot checked. According to the SOP starting materials samples were taken from every container and 100 % identity tests were performed.

The SOP "Packaging material sampling" was spot checked. AQL, inspection level II, was used for ampoule sampling. Defects were classified.

Stability testing

18 months stability data was available, but not reviewed by inspectors. One batch per year was placed for on-going stability studies.

Out of specification results (OOS)

The SOP (corporate) was applicable for all investigation of OOS results of raw materials and excipients, packaging materials, APIs and finished products obtained in QC laboratory as well as in stability studies.

This procedure was also applicable for microbiological OOS tests and sterility failure. It did not cover IPC activities in production.

There were different OOS registers for the chemical and microbiological labs. Registers were maintained on a month-wise basis.

Environmental monitoring of clean area (EM)

The SOP "Environmental monitoring in aseptic room using microbiological method" was discussed. Swab samples, air samples and settle plates were used for EM. Alert and action limits for the results of particulates and microbiological monitoring were defined and monthly trends of environmental monitoring were in place.

The "Environmental monitoring report of SVP filling room, December 2016" was reviewed and discussed.

Monitoring of PW and WFI

The SOP "Water quality routine monitoring" was spot checked. Alert limits were established 60 % from the specification. Sampling plan for drinking water, PW and WFI were in place. WFI critical sampling points at the return loop and storage tanks (SVP and LVP) were sampled and tested daily for endotoxins, conductivity and TOC.

Monthly and half yearly trends were performed and available for inspection. PW and WFI trends July – December 2016 were discussed.

Reference materials

The SOP "Reference standard and working standard" was spot checked.

Pharmacopoeia reference standard was used for Oxytocin impurity tests and a working standard for the assay test.

Working standards were prepared and dispensed by the R&D department in 12 amber glass vials. After opening each vial was required to be used within one month. Usage of reference materials were recorded in a log book.

Oxytocin reference materials were stored in the refrigerator at 2 – 8 ºC. T in the refrigerator was continuously recorded on charts. Charts were reviewed once per week. Temperature was controlled manually three times per day.

Stability studies

The SOP "Stability testing" was spot checked. Stability chambers Temperature and RH sensors were connected to the software and recorded continuously. Temperatures were checked manually three times per day. The chambers were equipped with a local sound alarm.

Retention samples

Finished product and APIs retention samples were stored in refrigerator at 2 – 8 ºC. T in the refrigerator was continuously recorded. T in the refrigerator was continuously recorded on charts. Charts were reviewed once per week. T was controlled manually three times per day.

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

Microbiology laboratory

Laboratory premises had separate rooms for positive controls, sterility tests, bioburden tests, media preparation and sterilization.

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 Sterile Preparation Plant (Unit III, Building A, Corima ampoule line) located at Jl. Industri Cimareme No.8, Desa Cimareme, Kecamatan Ngamprah, Kabupaten Bandung Barat – 40553, 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

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