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

Part 1	**General information**
Manufacturers details	
Name of manufacturer	Anhui Biochem Bio-pharmaceutical Co., Ltd - FPP site No. 30 Hongfeng Road, Hi-Tech Development Zone, Hefei City, Anhui Province, China Post code 230088 North latitude: N31°49′47.54″ East longitude: E117°11′8.72″
Corporate address of manufacturer	The 2nd floor of the Building 1, No. 30 Hongfeng Road, Hi-Tech Development Zone, Hefei City, Anhui Province Tel: +86 551 65232666 Fax: +86 551 65228225
Inspected site	
Name & address of inspected manufacturing site if different from that given above	As above
Workshop	OSD 1 Workshop
Building	Building 2
Inspection details	
Dates of inspection	22 - 26 July 2019
Type of inspection	Routine
Introduction	
Brief description of the manufacturing activities	Manufacturing, packaging, testing, storage and distribution for FPP.
General information about the company and site	Anhui Biochem Bio-pharmaceutical Co., Ltd is a pharmaceutical entity established in 2008 with a focus on the production of anti-HIV and anti-hepatitis B products. Anhui Biochem United Pharmaceutical Co. Ltd, is located at Hi-Tech development zone of Hefei city, the total land area is 72600 m^2 and factory area is 33000 m^2.
History	

Authority	**Date/s of inspection**	**Scope of inspection**	**Facility**
Hefei FDA	2014.07	Tablet/capsule	OSD 1
Namibia Medicine Regulator Council	2014.11	Tablet	OSD 1
Anhui	2015.04	Tablet/capsule	OSD 1

	Provincial FDA			
	Hefei FDA	2015.09	Tablet/capsule	OSD 1
	WHO inspection	2016.01	Tablet	OSD 1
	Hefei FDA	2016.07	Tablet/capsule	OSD 1
	WHO inspection	2016.08	Tablet	OSD 1
	Anhui Provincial FDA	2017.04	Tablet/capsule	OSD 1
	National GMP inspection	2018.07	Tablet	OSD 1
	Hefei FDA	2018.09	Tablet	OSD 1
	Kenya FDA	2019.05	Tablet	OSD 1

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	See Part 2 below
Restrictions	N/A
Out of scope	Products out of WHO prequalification
WHO products covered by the inspection	Lamivudine/Zidovudine tablet, film-coated 150 mg/300 mg
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
APS	Aseptic process simulation
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CFU	Colony-forming unit
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
GPT	Growth promotion test
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
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae
MFT	Media fill Test
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
SIP	Sterilization in place
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer
WFI	Water for injection

Part 2	**Summary of the findings and comments**

1. Quality system

Principle

Production and control operations were specified in written form and GMP requirements were essentially being met. Managerial responsibilities were specified in written job descriptions. Product and processes were monitored, and the results were reviewed as part of the approval process of batch release. Regular monitoring and reviews of the quality of pharmaceutical products were being conducted according to documented schedules and procedures.

Management review (MR)
SOP "Management review" was briefly discussed. MR was carried out quarterly. Standard agenda was specified. 2nd quarter: April - June 2019 MR minutes were briefly discussed.

Quality Risk Management (QRM)
"SOP for quality risk assessment" was briefly discussed.

The following tools were described in the SOP:
- FMEA
- FMECA
- FTA
- HACCP
- HAZOP
- PHA
- Risk Ranking and Filtering

The flow chart was briefly discussed:
- Risk assessment
  - Identification of the risk
  - Analysis of risk
  - Evaluation of risk
- Risk control
  - Risk reduction or risk acceptance
- Report
  - Output or result of the QRM
- Risk review

A risk assessment control strategy was performed for the product Lamivudine/Zidovudine Tablet, (film-coated 150 mg/300 mg).

Product Quality Review (PQR)
SOP "Annual product quality review" was briefly discussed. PQR reports were required to be completed by the end of February the following year.

SOP "SOP for CpK data analysis" was briefly discussed. "Minitab" software was used to calculate CpK. CpKs were applied for product critical quality attributes, including yield, assay, disintegration, dissolution, impurities etc.

Lamivudine/Zidovudine tablet, film-coated 150 mg/300 mg according to the WHO specifications and process was not manufactured, therefore PQR Lamivudine/Zidovudine tablet, film-coated 150 mg/300 mg according to the Chinese Pharmacopoeia was briefly discussed.

Deviations

SOP "Deviation investigation", its flow chart and logbooks for 2018 and 2019 were briefly discussed. The SOP was also applicable to QC deviations. According to the SOP, deviations related to production should be recorded in respective BMR/BPR.

Deviations were classified as:

- Critical
- Non-critical

Classification was performed by QA.

According to the SOP, deviations should be closed within 30 working days. If not possible, an extension should be approved by QP. Deviations were trended quarterly according to the root cause and discussed during management meeting.

A number of deviation records were briefly discussed.

Root Cause Analysis (RCA)

SOP "Root cause analysis" was briefly discussed. Tools specified in the SOP were: brain storming, 5 Why's and Ishikawa diagram.

Corrective actions and preventive actions (CAPA)

SOP "Corrective and preventive actions" was briefly discussed. The SOP was applicable to:

- Deviations
- OOS/OOT
- Recalls
- Complaints
- Rejection of materials
- Self-inspection
- External inspection
- PQR
- Management review

According to the SOP, CAPAs should be proposed by respective departments and approved by the QP. QA should follow-up on CAPA implementation and evaluate effectiveness. CAPA effectiveness checks were performed quarterly and annually.

Change control (CC)

"SOP for change control" was briefly discussed. This covered all change controls relating to the manufacture of products.

A number CC were briefly discussed.

Complaints

SOP "Customer complaints" and flow chart were briefly discussed. Quality department had overall responsibility for handling of complaints. According to the SOP, there was a complaint investigation committee which consisted of persons from:

- Quality department
- Production department
- Sales department
- Warehouse department
- Purchase department
- R&D department (depending of the nature of complaint)

No complaints were registered in 2018 and 2019.

Recalls

SOP "Product recall" was briefly discussed. Till the date of inspection there were no recalls registered by the company. QP and general manager were responsible for execution of recalls. The recalls were classified as:

- Class I: Could cause serious effect to health and should be executed within 24 hours.
- Class II: Could cause temporary problems to health and should be executed within 48 hours.
- Class III: No effect to health and should be executed within 72 hours.

According to the SOP, effectiveness of the recall (mock recall) should be evaluated every year. Mock recall was executed annually for domestic market and export market.

Self-inspection

"SOP for GMP self-inspection" was briefly discussed.

Two different types of self-inspections were documented:

- All departments were required to be inspected once per annum
- In addition, specific departments could be self-inspected more frequently, if required (changes etc.)

The self-inspection plan for 2018 was discussed. Prior to the self-inspection, training of the auditors was conducted.

Supplier management

"SOP for vendor evaluation and approval" was briefly discussed. QA had overall responsibility for the vendor approval process, together with other departments (Purchasing, QC, Production) for approving suppliers who could reliably supply starting and packaging materials and meet the established specifications.

The annual plan was reviewed in the December of each year.

Documentation
"SOP for document control" was briefly discussed.

There were 3 levels of documents:
Level I: Quality Manual and SMF
Level 11: Management procedures, specifications, analytical methods and manufacturing work instructions
Level 111: Operation procedures, BMRs/BPRs, labels, plan and reports
QA was responsible for the distribution of all approved documents. QA was required to stamp each page with a "Controlled Copy" stamp and a distribution number on the first page only. In the case of blank records (logbooks, analytical records) every page was stamped with a "Controlled Copy" stamp and a sequential number.

"SOP for record control" was briefly discussed.

The following specifications were briefly discussed:
- "Intermediate of Zidovudine and Lamivudine Tablet Specification (USP)"
- "Zidovudine and Lamivudine tablets (film-coated) Release Specification (USP)"

The BMRs and BPRs were issued by QA to Production according to "SOP for BMR/BPR control". A completed BMR/BPR were reviewed by the applicable production and QA production personnel by competing the "Batch Document Review" form which was part of the. The QP performed the final release of the batch using the "Final Product Release form.

Personnel
A number of job descriptions (JD) were checked.

Training
"SOP for training control" was briefly discussed.

Training was required when:
- A new employee was recruited
  - Company background, quality policy, safety, GMP, regulations.
  - Departmental training
  - Team training
- If employee changed position
  - Established a "Training Request Form" detailing the training requirements.

Re-training was performed annually according to the "Training Request Form" per position and "Training Plan".

Training records were retained by the administration department and were required to be retained indefinitely.

2. Production system

Access to production premises was to only authorized personnel. Production operations followed defined procedures. The layout of activities allowed for a logical flow from dispensing to final packaging.

The following was observed:

- Dispensing of materials for Lamivudine/Zidovudine tablet batch No XX
- Blending of Lamivudine/Zidovudine granules batch No XX
- Compression of Lamivudine/Zidovudine tablet batch No XX

Generally, activities were performed according to written instructions and any significant deviations from the initial protocol were recorded in BMRs and investigated, root causes were determined and CAPAs were implemented where necessary. In-process controls were performed separately by production and QA personnel at various stages of the production process. Checks on yields and reconciliation of material quantities were carried out. Batch records were observed to be available at the workstations and were completed contemporaneously.

3. Facilities and equipment system

Production premises were located, designed, constructed, adapted and maintained to suit the operations to be carried out. Floors were of smooth epoxy coating with appropriate covings and walls were of pharma grade sandwich panels. Premises including drains were cleaned and disinfected according to detailed written procedures, and records were maintained. Equipment contact surfaces were made of stainless steel. Dispensing UDAF, sifting mill and tray drier were inspected in detail. In general, equipment was seen to be maintained in good order.

General

Equipment was located, designed, constructed, adapted and maintained to suit the operations to be carried out. Balances and other measuring equipment were available for production and control operations and were calibrated on a scheduled basis. Calibration due-date labels were attached to the equipment. Current drawings of critical equipment and support systems were maintained.

SOP “Punches and dies management procedure” was briefly discussed. Punches and dies rotation was ensured.

Validation Master Plan (VMP)

The following documents were briefly discussed:

- SOP “Validation management”. SOP specified topics to be covered by validation and general approach to the validation. SOP also specified re-validation/qualification frequency.
- “Validation Master Plan”. VMP listed all validations to be performed.

Cleaning validation

SOP "Cleaning validation control" was briefly discussed. According to the SOP - Rinse, contact plates, swab and "visually clean" sampling methods were listed. Sampling methods were selected based on type of equipment.

Validation protocol and report for Zidovudine/Lamivudine tablets were discussed. Worst case approach was used and was established based on 10 ppm and solubility in water. The study covered also dirty equipment hold time. Swab recovery studies were carried out for SS, silicone, Teflon, PMMA (Polymethyl methacrylate) surfaces. As an example, blender was selected for the performed study evaluation. Samples were analyzed using HPLC method.

Validation protocol and report clean equipment hold time studies were briefly discussed. The results supported a 7-day clean equipment hold time.

Hold time studies

The following hold time studies were performed, protocols and reports were briefly checked:

- Uncoated and coated Lamivudine/Zidovudine tablet 150 mg/300 mg.
- Granules.

Laboratory premises

The Quality Control laboratories (including physico-chemical and microbiology laboratory, stability chambers, retention sample room and the auxiliary areas) were situated on the 3rd floor of building 3. Laboratory premises were quite old and therefore a new QC laboratory was under construction. The company presented to the inspector's laboratory equipment/instrument re-location schedule.

Laboratory equipment

SOP "Electronic data" was briefly discussed. The SOP explained:

- Back-up
- Data restoration
- Archiving
- Disaster management
- Printing of electronic data

SOP "Laboratory data management" was briefly discussed. There were 4 user levels specified.

HLPCs, GCs and other laboratory equipment/instruments validation protocols/reports including software and hardware were not checked during inspection because all laboratory equipment/instruments will be moved to the new laboratory and re-validation will be performed. This should be checked during the next inspection.

The inspector visited the R&D laboratory. It was noted that R&D HPLC and GC instruments connected to the OpenLabs CDS ChemStation edition software were audit trail enabled.

SOP "Computerized system management" was briefly discussed. The SOP explained password policy. SOP also specified that computerized systems should be reviewed annually to confirm that the system remains in validated status or determine the need for revalidation.

The following laboratory instruments calibration procedures and records were checked:
- HPLC
- UV (BC-02-013
- IR
- Dissolution
- GC
- Analytical balance

HPLC grade water was produced by Hitech Lab water purification system. Conductivity was monitored on-line; TOC analyses was performed weekly off-line.

4. Laboratory control system

Laboratory operations were well recorded and controlled. Interviewed personnel were professional and knowledgeable.

Out of specification results

SOP "OOS/OOT", flow chart and registers for 2018 and 2019 were briefly discussed. The SOP was applicable for physicochemical and microbial tests including packaging materials, raw materials, in-process tests and bulk products.

A number of OOS were briefly discussed.

The following SOPs were briefly discussed:
- SOP "Product release control" and its flow chart.
- "SOP for QC records".
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Lamivudine/Zidovudine tablet, film-coated 150 mg/300 mg batch No. XX analytical raw data (Chinese Pharmacopoeia) was cross-checked with meta data, equipment usage logbooks and standards usage logbooks:
- Standard test procedure "Lamivudine/Zidovudine tablets (film-coated tablets)
- Identification by HPLC No XX (assay test)
- Dissolution by HPLC No XX, balance No XX,
- Zidovudine/Lamivudine working standard XX (ref standard I) and YY (ref standard II).
- Reference solutions prepared on XX
- Dissolution test performed on XX
- Related substances tested together with assay HPLC No XX. Column No XX, balance No XX, balance YY. Test date: XX
  Note: No discrepancies were noted.

SOP "Raw materials sampling" was briefly discussed. NIR identification was performed for each container of raw materials. Maximum XX containers were pooled to prepare the composite sample, this procedure was supported by RA.

Sampling of components
SOP "Packaging materials sampling" was briefly discussed. The SOP was applicable to the sampling of primary and secondary packaging materials, printed packaging materials (labels). Sampling of the primary packaging materials was done according to the AQL. Defects were specified as critical, major and minor.

Reference standards
SOP "Working standards (WS)" was briefly discussed. WS were qualified against pharmacopoeia standards. Lamivudine WS batch No XX qualification report and analytical raw data were briefly discussed. Reference standards were stored in a refrigerator at 2 - 8 ℃. Temperature was checked and recorded twice per day. Working standards were dispensed in single use amber color vials.

Retention samples
Retention samples were stored for the expiry date + 1 year. Lamivudine/Zidovudine tablet, film-coated 150 mg/300 mg was not manufactured according to the PQ approved process and specifications. Therefore, retention samples were not available. Retention samples for local market were presented to the inspector.

Stability studies
Ongoing stability studies for Lamivudine/Zidovudine tablet, film-coated 150 mg/300 mg manufactured according to the PQ approved process and specifications were not available as these batches had not been manufactured. Studies were finalized at 36 M period.

Microbiology laboratory
The Microbiology laboratory had been separated from the Chemistry laboratory. Access was restricted to authorized personnel only. The laboratory activities, such as media, equipment preparation, testing and enumeration of microorganisms was segregated. There were appropriate entry and exit procedures, including gowning procedures.

Media was prepared in-house as stipulated in "SOP for media and diluents". The commercial dehydrated media was stored under appropriate conditions as recommended by the manufacturer. Media was prepared according to the manufacturer's instructions. Growth promotion testing was done on all media on every batch. The performance of the media was checked with regard to recovery of the target organisms.

Reference cultures were used for establishing acceptable performance of all media according to SOP "Culture management procedures". Reference cultures used were from the Chinese Medical Culture Collection. Traceability to the international collection could not be demonstrated as no CoAs were available. Working stock solutions were used for not more than five generations/passages.

An environmental monitoring program was in place.

5. Materials system

The receiving and dispatch bays were separated and protected from the weather.

The following procedures were briefly discussed:
- "SOP for warehouse control".
- "SOP for materials and product code control".

SOP detailed the allocation of the in-house batch number and material code.

Sampling

Sampling of raw materials was performed by QC in a separate sampling area. The HVAC system in the sampling area was not operational on an ongoing basis. Procedures for start-up and shutdown of the AHU were in place. Records were checked.

"SOP for sampling room management procedures" indicated that when the AHU was switched on, a period of 30 minutes was required before entering the sampling area.

The cleaning status of the room was required to be checked first before sampling. The disinfectants used were rotated on a monthly basis.

If sampling a different material, required to clean the sampling room and change clothing.
Logbooks required to be completed - Personnel access, PD, User, Cleaning and Disinfectant, HVAC.

The following were briefly discussed:
- "SOP for the air conditioning unit using and maintenance".
- "Air conditioning unit in buildings X and Y switch off/switch on risk assessment report"
- "Re-qualification protocol and report for the HVAC system in the building X" was briefly discussed.

Storage

Building X

Building X housed the following:
- Sampling area
- Storage of raw materials (API and excipients) and finished product.

Segregation was provided for the storage of:
- Rejected material
- Returns of raw materials from production
- Partials of released finished product (used as promotional material by marketing).

The storage area was clean, dry and sufficiently lit and maintained within acceptable temperature and humidity limits. Temperature and humidity at each location was monitored and recorded manually, twice a day, morning and afternoon.

Building Y
Building Y housed the following:
- Sampling area
- Storage area for primary packaging
  Note: Printed packaging materials were housed in a fenced off area.
- Storage area for secondary packaging
- Storage area for finished product
- Storage area for R&D raw materials
- Storage in a cold room
- Storage area for rejected products

SOP "Validation of temperature and humidity" and T and RH humidity mapping study for warehouse No X (finished product and raw materials) were briefly discussed. T and RH mapping was performed following WHO guidelines.

Packaging materials
Lamivudine/Zidovudine tablet, film-coated 150 mg/300 mg were packed in HDPE bottles, manufactured at XX. Quality agreement with XX company was briefly discussed

6. Packaging and labelling system
Both primary and secondary packaging lines for the OSD 1 manufacturing area for Lamivudine/Zidovudine tablet, film-coated 150 mg/300 mg were fully automated with adequate in-process checks to ensure correct packaging and labelling. The line was redesigned to prevent mix-ups following previous WHO inspection. Packaging and labelling for lamivudine and zidovudine was observed.

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, ***Anhui Biochem Bio-pharmaceutical Co., Ltd - FPP*** site, located at ***No. 30 Hongfeng Road, Hi-Tech Development Zone, Hefei City, Anhui Province, China*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines.

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 WHO Guidelines referenced in the inspection report

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO TRS No. 986, Annex 2***
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/
2. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2. ***Short name: WHO GMP for APIs*** or ***TRS No. 957, Annex 2***
   http://www.who.int/medicines/publications/44threport/en/

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

5. 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 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 GPPQCL Guidelines or ***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 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 TRS No. 996, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

23. WHO guidance on 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 guidance on Stability testing or WHO TRS No 1010, Annex 10**
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