20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

Prequalification Team Inspection services
WHO INSPECTION REPORT
Active Pharmaceutical Ingredients

Part 1	**General information**
Manufacturers details	
Name of manufacturer	Anhui Biochem United Pharmaceutical Co., Ltd (API site) North latitude: N33˚13'23.64" East longitude: E115˚36'22.2" D-U-N-S: 528178613
Corporate address of manufacturer	Zone B, Innovation Avenue, Taihe Industrial Park, Anhui, China 236604 Tel: + 86 558 2939161 Fax: + 86 558 2939161
Inspected Site	
Name & address of inspected manufacturing site if different from that given above	Anhui Biochem United Pharmaceutical Co., Ltd (API site) Zone B, Innovation Avenue, Taihe Industrial Park, Anhui, China (Zip Code: 236604)
Building	No 1, 3 and 5
Workshops	No 1, 3, 7 and 8
Inspection details	
Dates of inspection	15 – 19 July 2019
Type of inspection	Routine
Introduction	
Brief description of the manufacturing activities	Production and quality control of intermediates and finished non-sterile APIs. No toxic or hazardous substances were handled or manufactured.
General information about the company and site	The Anhui Biochem United Pharmaceutical Co., Ltd manufacturing site is located at Zone B, Innovation Avenue, Taihe Industrial Park, Anhui, Peoples Republic of China. The company had a land area of 84 463 m^2. The construction area was 64 346 m^2. There was a total of 492 employees (Production 302 and QA/QC 53). The following APIs and their intermediates were manufactured at the site: • Lamivudine (3TC) • Ritonavir (RTV) • Zidovudine (AZT) • Nevirapine (NVP) • Lopinavir (LPV)

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

- Lafutidine
- Entecavir
- Tenofovir disoproxil fumarate (TDF)
- Emtricitabine (FTC)
- Efavirenz (EFV)

</td></tr>
<tr><td>History</td><td>

<table>
<tr><th>Authority</th><th>Date/s of inspection</th><th>Scope of inspection</th></tr>
<tr><td>ANVISA</td><td>June 2014</td><td>Lamivudine</td></tr>
<tr><td>WHO PQ</td><td>January 2016</td><td>Lamivudine and Zidovudine</td></tr>
<tr><td>CFDA</td><td>June 2017</td><td>Entecavir</td></tr>
<tr><td>CFDA</td><td>September 2017</td><td>Lamivudine</td></tr>
<tr><td>CFDA</td><td>January 2019</td><td>Zidovudine and Emtricitabine</td></tr>
<tr><td>ANVISA</td><td>April 2019</td><td>Lamivudine (Recertification)</td></tr>
</table>

</td></tr>
<tr><td colspan="2">Brief report of inspection activities undertaken – Scope and limitations</td></tr>
<tr><td>Areas inspected</td><td>The inspection covered the following areas: Workshops, utilities, warehousing, solvent storage, production blocks, analytical and microbiological laboratories used in the manufacture of lamivudine, zidovudine and emtricitabine intermediates.</td></tr>
<tr><td>Restrictions</td><td>N/A</td></tr>
<tr><td>Out of scope</td><td>Parts of the site not concerned with the manufacture of the above APIs and intermediate were not inspected.</td></tr>
<tr><td>WHO products numbers related to this the inspection</td><td>

- Emtricitabine **intermediate**
- Lamivudine anhydrous **intermediate**
- Lamivudine anhydrous **intermediate**
- Zidovudine **API**
- Lamivudine anhydrous **API**

</td></tr>
<tr><td>Abbreviations</td><td>Meaning</td></tr>
<tr><td>ADE</td><td>Acceptable daily exposure</td></tr>
<tr><td>ADR</td><td>Adverse drug reaction</td></tr>
<tr><td>AHU</td><td>Air handling unit</td></tr>
<tr><td>ALCOA</td><td>Attributable, legible, contemporaneous, original and accurate</td></tr>
<tr><td>API</td><td>Active pharmaceutical ingredient</td></tr>
<tr><td>APQR</td><td>Annual product quality review</td></tr>
<tr><td>AQL</td><td>Acceptance quality limit</td></tr>
<tr><td>BMR</td><td>Batch manufacturing record</td></tr>
<tr><td>BPR</td><td>Batch production record</td></tr>
<tr><td>CAPA</td><td>Corrective and preventive action</td></tr>
<tr><td>CC</td><td>Change control</td></tr>
<tr><td>CCEA</td><td>Complete, consistent, enduring, available</td></tr>
<tr><td>CFU</td><td>Colony-forming unit</td></tr>
<tr><td>CIP</td><td>Cleaning in place</td></tr>
</table>

CoA	Certificate of analysis
Cpk	Process capability index
DQ	Design qualification
EDI	Electronic deionization
EHS	Environment, health and safety
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FTA	Fault tree analysis
GMP	Good manufacturing practices
GPT	Growth promotion test
HACCP	Hazard analysis critical control point
HAZOP	Hazard and operability study
HEPA	High efficiency particulate air
HPLC	High-performance liquid chromatography (or high-performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
ICH	International Council for Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
IQ	Installation qualification
KPI	Key performance indicators
LAF	Laminar air flow
LIMS	Laboratory information management system
LOD	Limit of detection
LOQ	Limit of quantification
MACO	Maximum allowable carry over
MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae
MR	Management review
NC	Non-conformity
NCA	National control authority
NCL	National control laboratory
NRA	National regulatory agency
OMCL	Official Medicines Control Laboratory
OOS	Out of specification
OOT	Out of trend
OQ	Operational qualification
PDE	Permitted daily exposure
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
RH	Relative humidity
RO	Reverse osmosis
RPN	Risk priority number
SMF	Site master file
SOP	Standard operating procedure
UPS	Uninterrupted power supply
URS	User requirements specifications
USP	United States Pharmacopoeia
UV	Ultraviolet-visible spectrophotometer
WS	Working standard

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 specified procedure.

Management review (MR)

SOP “Management review of quality system” and “Report of quality system in the fourth quarter of 2018” were briefly discussed. MR was performed quarterly. Standard agenda was specified in SOP and according to the report followed. MR was detailed document however was missing current expectations listed in section “Deviations”.

Product Quality Review (PQR)

SOP “Management procedure for annual quality review” was briefly discussed. Deadline to prepare PQR was specified as end of March the following year for batches manufactured the previous year (1 January till 31 December).

PQR reports of Lamivudine API, Zidovudine API and Zidovudine starting material 2018 was briefly discussed.

Documentation and records

The following documents were briefly discussed:

- "SOP for document management". If no changes, review period for documents was specified as 3 years.
- "SOP for record management".

Specifications for the starting material for Zidovudine and Zidovudine API were briefly discussed.

Quality Risk Management (QRM)

SOP "Quality Risk Management" was briefly discussed. The SOP was applicable to all the activities related to quality. According to the SOP the following tools could be used for QRM:

- Failure mode effect analysis (FMEA)
  Note: FMEA using SOP-QA-048 Version No. 00 (Valid date 2019-04-30)
- Hazard analysis and critical control points (HACCP)
- Hazard and operability analysis (HAZOP)
- Preliminary hazard analysis (PHA)
- Fishbone
- Checklist
- Process flow
- Brainstorm

The frequency of review was according to the risk level. At the end of the quarter, risk assessments in the previous period were required to be reviewed.

A number of RAs were briefly discussed.

Deviations

SOP "Investigation on deviation", its flow chart and register were briefly discussed. According to the SOP trending of deviations should be performed quarterly and included in the management review. Deviations were approved by Quality Manager. According the SOP, the investigation should be finalized in 20 working days. Trending was done according to the root cause.

Two levels of deviations were specified:

- Critical
- Minor

A number of deviation investigation reports were briefly discussed.

Corrective actions and preventive actions (CAPA)
SOP "Corrective actions and preventive actions", its flow chart and registers for 2018 and 2019 were briefly discussed. SOP was applicable to QMS of all departments.

Sources of defects and problems included, but not limited to:
- Deviations
- OOS
- Recalls
- Complaints
- Rejections
- Defects in internal or external audit inspections
- Product quality reviews
- Quality management reviews
- Risk assessments

Change control (CC)
SOP "Change control" and its flow chart were briefly discussed. The procedure applied to all changes related to product, document, system, equipment, instrument etc. According to the SOP, RA should be performed for all type of changes. Changes were classified as major, moderate or minor. The procedure also provided for temporary changes where "the change is made for some reason but will then be restored to its existing state". The Quality department was responsible for evaluating the changes that needed to be registered. For products that were licensed abroad, the changes should be notified to the relevant foreign drug supervision department.

After evaluation by the respective departments, the Quality department determined whether to accept or reject the change. If the change was approved, a "Change execution record" was initiated. At the completion of the change, the Quality department organized with other relevant departments to conduct an evaluation and/or acceptance of the change. Final approval of CCs was done by QA Manager.

A number of change controls were briefly discussed.

Complaints
SOP "Handling procedure of customer complaints", its flow chart and registers for 2018 and 2019 were briefly discussed. According to the SOP, QA was responsible for handling of complaints. Complaints were classified as major and minor. Complaints were received by sales department and forwarded to QA for investigation. According to the SOP complains should be closed within 75 working days. Investigation should be done by 30 working days.

A number of complaint investigation records were briefly discussed.

Recalls

SOP "Product recall" was briefly discussed. Responsible person was Quality Manager. Recalls were classified as:

- Class I: Should be executed within 24 hours
- Class II: Should be executed within 48 hours
- Class III: Should be executed within 72 hours

Till the date of inspection there were not recalls. The SOP effectiveness was evaluated by the mock recall. According to the SOP, mock recall should be carried out every year.

Personnel

Training

SOP "SOP of training management" was briefly discussed.

Training/retraining was conducted when:

- New personnel joined the company
- Personnel changed position
- Personnel on extended vacation/absent for more than 3 months
- Once per annum (Training matrix per position)
- Procedures were updated

Training was categorized as:

Level I: Face to face training
Level 11: Operation training - Practical assessment
Level 111: Questionnaire (Pass mark ≥ 90 %)
Level 1V: Report/Synopsis

A training matrix indicating the type of training was presented for the microbiologist position.

Data integrity policy

"SOP for data integrity" was implemented IN ma and briefly discussed with regards "ALCOA" principles.

2. Production system

Production operations followed defined procedures. Significant deviations from the initial protocol were recorded and investigated, root causes were determined and CAPAs were implemented where necessary. Checks on yields and reconciliation of quantities were carried out. Access to production premises was restricted to authorized personnel.

The production process for Zidovudine API in Building 5 Workshop 8 was followed. Generally, the production process was observed to be consistent with the documented flow process. Equipment such as reactors, centrifuges, solvent pipes, were appropriately identified and maintained in a proper state. Pressure gauges and temperature probes were appropriately calibrated. Qualification records of one

of the solvent tanks was briefly discussed. Batch records were available at the workstations and indicated the process instructions, time limits for critical reaction steps and in-process controls for intermediates where applicable. At the time of inspection, batch No. XX was undergoing distillation.

Batch Production Record (BPR)
The Zidovudine BMR was briefly discussed.

Rejection and re-use of materials
SOP "Management of rejected materials" was briefly discussed.

Blending of batches
SOP "Blending and packaging procedure for intermediates and API" was briefly discussed. Retest date of the blend was established based on the oldest lot/batch in the blend.

Reprocessing and reworking
SOP "Re-work and re-production of intermediate and API" was briefly discussed. According to the SOP re-working was not allowed for APIs according to the WHO specification. The SOP stated that reworked batches would be subjected to process validation and stability studies.

Procedure for reprocessing: Deviation investigation → Approval by the quality department → Reprocessing according to the production procedure.

If a batch was to be reprocessed, the established manufacturing process was to be followed. If a batch was to be reworked, a rework document was to be initiated by production and R&D and approved by QA.

Recovery of solvents and mother liquor
"SOP for mother liquor recycle LAM-II post" was briefly discussed.

- Recovered solvents were collected in dedicated tanks.
- Only allowed in the same step/same product.
- Recovered solvents were tested according to their own specification.

SOP "Management procedure of recovered solvents" and SOP "Management procedure of recovered solid materials" stated that recovered solvents and solid materials were not used to produce APIs according to the WHO specification.

Validation Master Plan (VMP)

VMP for 2019 was briefly discussed. VMP was applicable to:

- Facilities
- Instruments
- Equipment
- Production process
- Test methods
- Cleaning programs
- Computerized systems

The following SOPs were briefly discussed:

- "SOP of validation management"
- "SOP for validation of manufacturing process".

Cleaning validation

Cleaning validation SOP, protocol and report for ZDV reactor, equipment No XX were briefly discussed. The company mentioned that this piece of equipment would be shared between different products, however no other products besides Zidovudine API had been manufactured in this reactor by the time of inspection. A risk assessment was performed for the cleaning validation. Visual cleanliness, microbial limit and 10 ppm criteria were chosen for the cleaning validation studies. Sampling locations from the equipment were pictorially identified and appeared to represent the hard to clean spots in the reactor. Both rinse and swab samples were taken as appropriate, and recovery studies the rinse and for the swab samples were conducted. It was noted however that the company had not yet adopted the health-based exposure limits in their cleaning validation studies.

3. Facilities and equipment system

Production premises were located, designed, constructed, adapted and maintained to suit the operations to be carried out. Premises were cleaned according to written procedures, records were maintained. Production buildings were seen to be clean and in good order. Labels attached to the equipment clearly indicated equipment identification numbers, qualification status and due date.

Utilities

- Purified water system
  The feedwater source was bore well. Purified water was generated through double reverse osmosis. A re-circulation loop with XX user points was maintained. Sampling points for supply and return purified water was clearly identified. Sanitization was performed on a monthly basis using hot water at 80 ^{0}C for 2 hours.
- HVAC system
  The AHU for the grade D area, equipment ID XX for Zidovudine final purification process was briefly inspected. A single AHU supplied filtered air to the grade D area. The filtration system comprised of pre and F8 filters in the plenum with terminal HEPA filters installed above the rooms. Procedures were in place for routine cleaning and change of pre and F8 filters. HEPA filters were replaced every 2 years.

- Compressed air system
  Nitrogen and compressed air were used in filtration systems and operation of the jet mill among others. Qualification of both systems was conducted at initial installation and required to be repeated every 3 years. Key parameters tested during the qualification included physical, chemical and microbial parameters. These were observed to be within pre-defined limits.

Laboratory premises
Chemical laboratory facilities were of a suitable size, construction and location and were designed to suit the functions and operations to be conducted. Chemical/instrumental laboratories were not separated from the microbiological laboratory. The microbiological laboratory was not of a suitable size as certain equipment was housed in the Chemical laboratories.

Laboratory equipment
Chemistry laboratory was well equipped with equipment required for analysis.

SOP "Operation, calibration and maintenance procedure for analytical balance ID XX" was briefly discussed. Daily calibration was performed using 3 different standard weights, weekly calibrations used 5 different standard weighs according to the balance weighing range. Monthly calibration was performed according to the USP chapters 41 and 1251.

Internal qualification records were seen for:
- HPLC Agilent ID XX performed according to the OMCL guideline
- Polarimeter ID XX
- GC Agilent ID XX performed according to the OMCL guideline

4. Laboratory control system
SOP "Management of electronic data in QC" was briefly discussed. SOP explained back-up, archiving and management of computers and workstations. SOP specified 4 access levels to XX software. For YY software 3 access levels were specified. Back-up, data restoration and archiving exercises were regularly performed.

"SOP for Electronic data" was briefly discussed. SOP explained disaster management procedure.

SOP "Release for intermediate and API" and SOP "Procedure for QC chromatography" were briefly discussed. Manual integration was allowed. Request for manual integration should be approved by supervisor.

Out of specification/Out of trend
SOP "Investigation of OOS/OOT" was briefly discussed.

Stability monitoring
Stability samples were stored in qualified chambers, T and RH was checked manually 4 times per day. T was automatically recorded every 30 minutes, print outs were checked and compared with manual records. Chambers were equipped with sound, light and text message alarm system. It was said that alarm system was challenged.

Reference materials
Reference materials were stored in refrigerator at 2 - 8 ºC. T in the refrigerator was checked and recorded manually 4 times per day. T was automatically recorded every hour, print outs were checked daily. Refrigerator was equipped with sound alarm system.
The characterization report/COA for working/in-house reference standard X, batch Y was verified.

The following SOPs were briefly discussed:
- SOP "Management of reference standard".
- SOP "Preparation, qualification, identification and storage of working standards and in-house reference standards for finished products (API)". Working standards (WS) were standardized against pharmacopeia standards. WS were dispensed in amber color vials.

Retention samples
Retention samples we stored in the same packaging system in which the API were stored. Retention samples storage was seen to be well organized.

Microbiology laboratory
SOP "Management of microbial laboratory" was briefly discussed. Cleaning and disinfection were performed at the end of each test and weekly. This was performed using 75 % isopropyl alcohol or 0.1 % bromo-geramine. The disinfectants were rotated monthly.

Reference cultures
The reference cultures were stored at - 40 °C ± 3 °C in the Stability Chamber Room due to the availability of an uninterrupted power supply (UPS). The following reference cultures were checked:
- Escherichia coli
- Staphylococcus aureus
- Pseudomonas aeruginosa
- Bacillus subtilis
- Aspergillus niger
- Candida albicans

The working stocks were not sub-cultured more than 5 passages (generations) from the original reference culture. A Biohazard Safety Hood Class A was used for the handling of reference cultures.

Incubators
A number of incubators IQ, OQ, PQ protocols/reports were briefly discussed. "SOP for analytical instruments" required instruments to be requalified if changes were required, otherwise instruments were requalified annually.

Autoclaves
There were 4 vertical autoclaves used for the sterilization of media, equipment, garments and decontamination.

IQ, OQ, PQ protocol/report for vertical pressure autoclave ID XX was briefly discussed.

Purified water
"Product quality review report for purified water for 2018 was briefly discussed. Purified water was tested per the USP:

- pH
- Nitrate
- Nitrite
- Microbial limits
- TOC
- Non-volatile matter
- Heavy metals
- Ammonia
- Conductivity

Action and alert limits were specified.

Environmental monitoring (EM)
An environmental program was in place in the clean rooms and Class A work benches.

5. Materials system
Receipt, management and storage of raw materials at the warehouse was managed according to "SOP of reception and release for materials". Generally, materials were sourced from qualified suppliers, appropriate checks were done during receipt. Temperature in the storage areas was controlled using AC. Solvents in drums were stored in dedicated warehouse. The status of materials was managed using yellow stickers (quarantine) and green stickers (approved). A dedicated sampling area, consisting of a laminar booth and fume hood was available for sampling solid raw materials.

SOP "Product return and change", its flow chart and registers for 2018 and 2019 were briefly discussed.

Supplier management

SOP "Supplier quality management" and its flow chart were briefly discussed. According to the SOP, on-site audits had to be performed for key starting materials, primary packaging materials and purchased intermediates. Suppliers audit schedules (on-site and questionnaire based) for 2018 and 2019 were presented to inspectors. The list of approved suppliers for starting material XX was verified in the warehouse.

Quality agreement with solvent broker XX company was briefly discussed.

6. Packaging and labelling system

No packaging/labelling operations were carried out during the inspection. The following SOPs were briefly discussed:

- "Packaging of Lamivudine".
- "Management of labels and seals". Labels were printed in house by QA or sales department. Labels were verified by QA.

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 United Pharmaceutical Co., Ltd (API site),*** located at ***Zone B, Innovation Avenue, Taihe Industrial Park, Anhui, China*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines for APIs.

All the non-compliances observed during the inspection that were listed in the full report as well as those reflected in the WHOPIR, were addressed by the manufacturer, to a satisfactory level, prior to the publication of the WHOPIR

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.

Part 4	**List of GMP Guidelines referenced in the inspection report**

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

2. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2

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

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

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

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

6. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Third Report Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 2.
   Short name: WHO TRS No. 1019, Annex 2
   https://apps.who.int/iris/bitstream/handle/10665/312316/9789241210287-eng.pdf?ua=1

7. Good manufacturing practices: guidelines on validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Third Report Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 3.
   Short name: WHO TRS No. 1019, Annex 3
   https://apps.who.int/iris/bitstream/handle/10665/312316/9789241210287-eng.pdf?ua=1

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

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 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

11. 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

12. 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

13. 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 (WH0.O 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

14. 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

15. 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/

16. 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/

17. 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

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

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

20. WHO Recommendations for quality requirements when plant-derived artemisin is used as a starting material in the production of antimalarial active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 6.
Short name: WHO TRS No. 992, Annex 6
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

21. Guidance on good data and record management practices. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 5.
Short name: WHO GDRMP guidance or **WHO TRS No. 996, Annex 5**
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf

22. WHO general guidance on variations to multisource pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10.
Short name: WHO Multisource guidance or **WHO TRS No. 996, Annex 10**
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

23. 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**
https://extranet.who.int/prequal/sites/default/files/documents/TRS1010_Annex10.pdf