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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
Finished Product Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	Zhejiang Hisun Pharmaceutical Co., Ltd 1 Haizheng Avenue, Jiaojiang District, Taizhou City, Zhejiang Province, P.R.C. Post code: 318000 Longitude (121°47'), Latitude (28°67') DUNS number: 654211754
Corporate address of manufacturer	46 Waisha Road, Jiaojiang District, Taizhou City, Zhejiang Province, P.R.C. Telephone Number: +86-576-88827900 Fax Number: +86 576 88827 887
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Zhejiang Hisun Pharmaceutical Co., Ltd 1 Haizheng Avenue, Jiaojiang District, Taizhou City, Zhejiang Province, P.R.C. East Campus Post code: 318000 Longitude (121°47'), Latitude (28°67') DUNS number: 654211754
Unit / block / workshop number	Workshop in building E03 of East Campus QC laboratory – building WS05 of Waisha Campus Address: 46 Waisha Road, Jiaojiang District, Taizhou City, Zhejiang Province, P.R.C. Post code: 318000 Longitude (121°46'), Latitude (28°68') DUNS number: 654211754
Inspection details	
Dates of inspection	22 – 28 March 2019
Type of inspection	Routine
Introduction	
Brief description of the manufacturing activities	East Campus: The production of FPPs, including Tablets, Hard capsules Waisha Campus – Quality Control
General information about the company and site	Zhejiang Hisun Pharmaceutical Co., Ltd. (hereinafter Hisun) was founded in 1956, being a company listed as a state-owned corporation in Shanghai A Share Stock Exchange in year 2000. Hisun is authorized by the Chinese Competent Authority and inspected regularly. A pharmaceutical production license has been issued by NMPA (China Authority). Hisun exports more than 80% of API products to over 70 countries and regions.

<table>
<tr><td></td><td>Hisun Taizhou site consists of three campuses within short driving distances.</td></tr>
<tr><td>History</td><td>The site had been inspected by the following authorities:
<table>
<tr><th>Authority</th><th>Date/s of inspection</th><th>Scope of inspection</th><th>Facility/block/unit covered by inspection</th></tr>
<tr><td>CFDA (China)</td><td>June 20-22, 2014</td><td>API</td><td>Waisha Campus, Yantou Campus</td></tr>
<tr><td>Germany Authority</td><td>July 9-16, 2014</td><td>API & FPP</td><td>Waisha Campus, East Campus, Yantou Campus</td></tr>
<tr><td>MCC/South African</td><td>August 18-20, 2014</td><td>API & FPP</td><td>Waisha Campus, East Campus, Yantou Campus</td></tr>
<tr><td>WHO</td><td>September 9-13, 2014</td><td>API & FPP</td><td>Waisha Campus, East Campus, Yantou Campus</td></tr>
<tr><td>US FDA</td><td>March 2-7, 2015</td><td>API & FPP</td><td>Waisha Campus, East Campus, Yantou Campus</td></tr>
<tr><td>WHO</td><td>March 13-20, 2015</td><td>API & FPP</td><td>Waisha Campus, East Campus, Yantou Campus</td></tr>
<tr><td>CFDA (China)</td><td>April 20-25, 2015</td><td>API & FPP</td><td>Waisha Campus, East Campus, Yantou Campus</td></tr>
<tr><td>Cofepris (Mexico)</td><td>May 25-29, 2015</td><td>API</td><td>Waisha Campus, Yantou Campus</td></tr>
<tr><td>CFDA (China)</td><td>October 22-24, 2015</td><td>API</td><td>Waisha Campus, Yantou Campus</td></tr>
<tr><td>CFDA (China)</td><td>November 10-15, 2015</td><td>API & FPP</td><td>Waisha Campus, East Campus, Yantou Campus</td></tr>
<tr><td>Cofepris (Mexico)</td><td>January 25-29, 2016</td><td>API</td><td>Waisha Campus, Yantou Campus</td></tr>
<tr><td>ANVISA (Brazil)</td><td>March 21-25, 2016</td><td>API</td><td>Waisha Campus, Yantou Campus</td></tr>
<tr><td>CFDA (China)</td><td>March 30-April 1, 2016</td><td>API</td><td>Waisha Campus, Yantou Campus</td></tr>
<tr><td>Cofepris (Mexico)</td><td>April 18-29, 2016</td><td>API</td><td>Waisha Campus, Yantou Campus</td></tr>
<tr><td>Spain-Demark-WHO Joint</td><td>May 30 to June 3, 2016 (Re-inspected in April 2018)</td><td>API & FPP</td><td>Waisha Campus, East Campus, Yantou Campus</td></tr>
<tr><td>Health Canada (Canada)</td><td>July 18-29, 2016</td><td>API & FPP</td><td>Waisha Campus, East Campus, Yantou Campus</td></tr>
<tr><td>ANVISA (Brazil)</td><td>October 24-28, 2016</td><td>API</td><td>Waisha Campus, Yantou Campus</td></tr>
<tr><td>CFDA</td><td>November</td><td>API</td><td>Waisha Campus, Yantou</td></tr>
</table></td></tr>
</table>

	(China)	31 - December 2, 2016		Campus
	US FDA	January 16-19, 2017	API & FPP	Waisha Campus, East Campus, Yantou Campus
	CFDA (China)	February 22-25, 2017	API	Waisha Campus, Yantou Campus
	J-MAFF (Japan)	March 8-10, 2017	API	Waisha Campus, Yantou Campus
	Cofepris (Mexico)	March 20-24, 2017	API	Waisha Campus, Yantou Campus
	CFDA (China)	April 24-26, 2017	API	Waisha Campus, Yantou Campus
	Health Canada (Canada)-TGA (Australia) Joint	May 22 - June 2, 2017	API & FPP	Waisha Campus, East Campus, Yantou Campus
	Cofepris (Mexico)	June 5-9, 2017	API	Waisha Campus, Yantou Campus
	US FDA	August 7-11, 2017	API & FPP	Waisha Campus, East Campus, Yantou Campus
	CFDA (China)	August 24-27, 2017	API	Waisha Campus, Yantou Campus
	CFDA (China)	August 29-31, 2017	API	Waisha Campus, Yantou Campus
	CFDA (China)	September 19-21, 2017	API & FPP	Waisha Campus, East Campus, Yantou Campus
	Cofepris (Mexico)	October 30-November 3, 2017	API	Waisha Campus, Yantou Campus
	CFDA (China)	December 1-3, 2017	API	Waisha Campus, Yantou Campus
	WHO	December 7-15, 2017	API & FPP	Waisha Campus, East Campus, Yantou Campus
	CFDA (China)	December 21-22, 26-27, 2017	API & FPP	Waisha Campus, East Campus, Yantou Campus
	CFDA (China)	December 21-27, January 7-12, 2018	API	Waisha Campus, Yantou Campus
	CFDA (China)	January 23-24, 2018	API	Waisha Campus, Yantou Campus

	Koshar	January 31, 2018	API	Waisha Campus, Yantou Campus
	AEMPS-VMD-DMA (Spain-UK-Demark) Joint	April 9-14, 2018	API & FPP	Waisha Campus, East Campus, Yantou Campus
	CFDA (China)	April 17-22, 2018	API & FPP	Waisha Campus, Yantou Campus
	CFDA (China)	June 25-30, 2018	API	Waisha Campus, Yantou Campus
	CFDA (China)	August 15-17, 2018	API	Waisha Campus, Yantou Campus
	CFDA (China)	August 21-23, 2018	FPP	Waisha Campus
	PMDA (Japan)	October 23-26, 2018	API	Waisha Campus, Yantou Campus
	WHO	December 4-7, 2018	FPP	Waisha Campus (TB357 -Levofloxacin Tablet, Film-coated 250mg TB358 - Levofloxacin Tablet, Film-coated 500mg)

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	See Part 2 below
Restrictions	N/A
Out of scope	Products out of scope of WHO PQ
WHO products covered by the inspection	• Cycloserine Capsules, hard 250mg • Moxifloxacin (hydrochloride) Tablet, Film-coated 400mg
Abbreviations	**Meaning**
ADE	Acceptable daily exposure
ADR	Adverse drug reaction
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APQR	Annual product quality review
APS	Aseptic process simulation
AQL	Acceptance quality limit
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CCEA	Complete, consistent, enduring, available
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
LoD	Loss in drying
MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae
MFT	Media fill Test
MR	Management review
NC	Non-conformity
NCA	National control authority
NCL	National control laboratory
NRA	National regulatory agency
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

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.

QA functions were arranged on various levels (Site, production units, product-wise etc.)

All three campuses were under the same quality system, with the same senior management. Testing for release and release procedure took place in Waisha campus where the headquarters of Taizhou Site are located.

Data integrity policy

The following SOPs were briefly discussed:

- "Data integrity management procedure". SOP was applicable to all GXP activities on the site, paper and electronic documents, and explained ALCOA+CCEA principles.
- "Computerized system backup and data migration management procedure". Daily and weekly backups were performed automatically.
- "Computerized system management procedure". SOP explained GXP computerized system different levels, classification and qualification requirements. Attachment "Computerized system list" was presented to the inspectors.
- "Disaster recovery management procedure".
- "Computerized system for data server management procedure". SOP listed servers available and used on site including servers log.
- "Computerized system user access management procedure in lab"

  The following additional documents were briefly discussed:
  - "User rights assignment of ECM (OpenLab)"
  - "Shimadzu LabSolutions server and client operation procedure"
  - "Lab computerized system user list format"
  - "Lab computerize system user access change request form"

Management review (MR)

The SOP was a Corporate level procedure. Quarterly review period was applied by the Taizhou Site; yearly period was defined for the Corporate level. Common reviews for APIs and dosage forms were drawn by the Taizhou Site. MR for 4th quarter 2018 was presented to the inspectors.

Quality Risk Management

The "Quality risk management procedure". Tools listed for RA were:

- Ishikawa diagram
- Flow chart
- Check list
- Risk ranking and filtering
- HAZOP
- HACCP
- FMEA
- FMECA
- FTA

According to the Company, FMEA was mainly used. Performed RAs register for workshop XX and RA schedule were presented to the inspectors.

Product Quality Review (PQR)

The "Product annual quality review management procedure" and SOP was briefly discussed. Cpk was used to evaluate process capability and applied for critical and quantitative parameters for intermediates and final APIs.

As products under the WHO PQ programme were not commercially manufactured, a PQR for Cycloserine Capsules 0.25 g for local market 01/01/2018 – 12/31/2018 was discussed as an example.

The following SOPs applicable to APIs and FFPs were briefly discussed:

- "Deviation management procedure". Deviations were trended every 3 months and annually.
- "Investigation tools – application management procedure". The following tools were used for root cause investigations:
    - Ishikawa diagram
    - 5 Why`s
    - Events flow analysis
    - Brain storming
    - Pareto diagram
- "Corrective and preventive action management procedure". CAPAs were trended biannually and annually. Trends for 2018 site were presented to inspectors.
- "Returned product management". Returns registers were presented to inspectors.
- "Complaint management procedure". Complaints were trended biannually and annually. Trends for 2018 were presented to the inspectors. Complaints were classified into 5 levels, level 1 being the most critical. Several complaint investigation reports were discussed.
- "Product recall procedure". The Company stated that there had been no recalls in the Site history. Five levels for product quality issues were defined.
- "Change control" was briefly discussed.

Documentation

Documents related to the manufacture of intermediates and FPPs were prepared, reviewed, approved and distributed according to written procedures. The SOPs were also displayed at appropriate points. The issuance, revision, superseding and withdrawal of documents were controlled with maintenance of revision histories. Documents coded as XX were common to APIs and FPPs sites.

The following SOPs were briefly discussed.

- "Drafting and management of documents". Documents were required to be reviewed:
- "Management procedure of quality stamp".
- "Issuing, recording, reviewing and archiving batch records". This SOP was applicable to FPP manufacturing in East and Waisha campuses. BMRs/BPRs were issued by QA.

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 following documents were briefly discussed:

- "Laundry procedure in class D area". PW was used for washing and rinsing of garments. Different laundry machines were used for garments and footwear.
- "Cross-contamination control procedure".

Written procedures were available for cleaning of production equipment, containing essential details and supported with photos, difficult-to-clean areas were marked. Procedures and instructions were provided in various documents.

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 and disinfected according to detailed written procedures, records were maintained. It was noted that over the last years the building E03 had not been in intensive use.

Inspectors visited starting material and packaging material warehouses, Cycloserine capsules and Moxifloxacin (hydrochloride) tablets production rooms. Production equipment was identifiable in the facility and in the documents.

Utilities E03 HVAC

Separate HVAC system were provided for 1st, 2nd, 3rd and 4th floors of the building inspectors visited.

The SOP "Technical manual for HVAC system of 302 workshop" was briefly discussed. Filters were replaced using bag-to bag procedure.

Layouts of E03 floors were available with pressure differentials.

Utilities E05 - purified water (PW)
Inspectors visited the PW system, located in building E05. PW was produced by one generation system: source water (city water) → sand filter → carbon filter → pretreatment → 1st RO → storage tank → 2nd RO → EDI.

PW was in continuous circulation at NMT 25 °C. T and return PW velocity was monitored on the return loop. Conductivity and T were monitored on-line at pretreatment water inlet to the 2nd RO, after the 2nd RO, and on the return loop. TOC was checked daily off-line.

Laboratory premises for QC analysis of APIs and FPPs were located at Waisha campus and were separated from production areas.

Laboratories were well equipped with instruments and software tools for managing analyses. HPLCs, GCs, IRs and UV were networked. Sufficient space was given to avoid mix-ups and cross-contamination. Adequate storage space was provided for samples, reference standards, solvents, reagents and records.

The following documents were briefly discussed:
- "Liquid chromatograph calibration procedure"
- "Liquid chromatograph calibration record". Calibration was performed by the Site calibration group.
- "Calibration procedure for Dissolution Apparatus (OQ). Dissolution equipment calibration kit was presented to inspectors.
- "Calibration record of electronic balance" (based on USP requirement – USP 41 and 1251). Calibration was performed by the Site calibration group ("instrument department") every six months. Analytical balances daily verification was carried out in the QC lab.

4. Laboratory control system
At Waisha campus, separate QC laboratories (chemical/instrumental and microbiological) were provided for APIs and FPPs.

Media plates for environmental monitoring were procured ready-made and sterile. The policy was to do growth promotion test on each batch. Results from monitoring clean room environment and purified water were trended.

Inspectors cross-checked Cycloserine capsules 0.25 mg, batch No XX some analytical raw data with equipment ID numbers and usage logs.

Cycloserine working reference standards were dispensed in amber vials and stored in deep freezer at T -15 – -25 °C.

The following documents were briefly discussed:

- "Management procedure for verification and review in laboratory" and annex "Authorized second person verifier list in QC laboratory". Audit trails for WHO products in MS Excel were requested from the Company, random cross-checks were carried out and no discrepancies noted.
- "Injection procedure for determination by GC/HPLC method"
- "Integration and processing method for chromatograms".
- "Management procedure of excel spreadsheet" and "Spreadsheet drafting and revising application form".
- "Lab unexpected event handling procedure". SOP was applicable to abnormal QC labs events, for example sample spillage, system suitability failure etc. Unexpected events were trended biannually and annually. Trends for 2018 were presented to inspectors.
- "Investigation procedure for OOS/OOT test results of chemical results". OOS/OOT results were trended biannually and annually. Trends related to APIs for 2018 were presented to inspectors. Several OOS were briefly discussed.
- "Investigation procedure for OOS/OOT for microbiology analysis. No OOS were recorded from 2017.
- "Sampling management procedure", applicable to sampling excipients, purchased APIs and packaging materials.

5. Materials system

Inspectors visited warehouses located on the 1st floor used for starting materials, packaging materials and finished materials.

Materials in the warehouses visited were stored under appropriate conditions and in orderly fashion to permit batch segregation and stock rotation.

Material management/reconciliation was handled manually on stock cards and using SAP system.

The SOP "Distribution procedure of raw materials and packaging materials" was briefly discussed.

6. Packaging and labelling system

Packaging and labelling was not carried out during inspection.

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, ***Zhejiang Hisun Pharmaceutical Co., Ltd East Campus*** located at ***1 Haizheng Avenue, Jiaojiang District, Taizhou City, Zhejiang 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.

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