World Health Organization

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 PUBLIC INSPECTION REPORT
of the FPP manufacturer

Part 1	**General information**
Manufacturers Details	
Company information	
Name of manufacturer	North China Pharm Co (NCPC) - New Preparation Branch Factory
Address	No. 115 Hainan Road, Shijiazhuang Economic & Technological Development Zone, Hebei, China. Zip Code: 050000 North latitude: 38°02'40.5" East longitude: 114°33'45.7" DUNS No.: 54-440-8358
Corporate address of manufacturer	No. 217-1, Heping East Road, Hebei, P.R. China Tel: +86-311-85528588-8937 Fax: +86-311-85528588-8935
Inspected site	
Address of inspected manufacturing site if different from that given above	As above
Unit/block/ plant number	Workshop 201
Inspection details	
Dates of inspection	14 - 18 January 2019
Type of inspection	Routine
Introduction	
Brief summary of the manufacturing activities	The main activity is the manufacturing, packaging, labelling, testing and storage of: • Soft capsules • Oral solutions • Granules • Tablets • Hard capsules • Lyophilized Powder for Injection

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

- Powder for Injection
- Small Volume Injections
- Eye drops
- Eye gels
- Psychotropic drugs

</td></tr>
<tr><td>General information about the company and site</td><td>NCPC New Preparation Branch Factory is located at No. 115 Hainan Road, Economic & Technological Development Zone, Shijiazhuang, Hebei.
NCPC New Preparation Branch Factory is part of North China Pharmaceutical Co., Ltd. (NCPC), which was established in 2011. The factory produces pharmaceutical and healthcare products. There are three manufacturing workshops on this site. Workshop 201 is used for the manufacture of sterile preparations, workshop 202 is used for the manufacture of oral dosage forms and workshop 203 is for the manufacture of healthcare products. There is no toxin or hazardous substances manufactured in this factory.</td></tr>
<tr><td>History</td><td>The previous inspection by WHO PQT was performed 1 - 5 February 2016.
The site was inspected by the following authorities:

<table>
<tr><th>Authority</th><th>Date/s of inspection</th></tr>
<tr><td>CFDA</td><td>2013-03</td></tr>
<tr><td>CFDA</td><td>2013-05</td></tr>
<tr><td>Province FDA</td><td>2014-05</td></tr>
<tr><td>WHO</td><td>2014-10</td></tr>
<tr><td>CFDA</td><td>2015-09</td></tr>
<tr><td>CFDA</td><td>2018-03</td></tr>
<tr><td>CFDA</td><td>2018-05</td></tr>
</table>
</td></tr>
<tr><td>Brief report of inspection activities undertaken</td><td></td></tr>
<tr><td>Scope and limitations</td><td></td></tr>
<tr><td>Areas inspected</td><td>See Part two below</td></tr>
<tr><td>Restrictions</td><td>N/A</td></tr>
<tr><td>Out of scope</td><td>Eye drops, Small Volume Injections, Lyophilized Powder for Injection</td></tr>
<tr><td>WHO product numbers covered by the inspection</td><td>

- Sterile Powders for solution for Injection g

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

Abbreviations		
	ADE	acceptable daily exposure
	AHU	air handling unit
	ALCOA	attributable, legible, contemporaneous, original and accurate
	API	active pharmaceutical ingredient

APQR	annual product quality review
AQL	acceptance quality limit
ATCC	American Type Culture Collection
BET	bacterial endotoxin test
BDL	below detection limit
BMR	batch manufacturing record
BPR	batch packaging record
CAPA	corrective actions and preventive actions
CC	change control
CFU	colony-forming unit
CoA	certificate of analysis
Cpk	process capability index
DQ	design qualification
EM	environmental monitoring
EU	endotoxin unit
FAT	factory acceptance test
FG	finished goods
FMEA	failure modes and effects analysis
FPP	finished pharmaceutical product
FTA	fault tree analysis
FTIR	Fourier transform infrared spectrometer
GC	gas chromatograph
GMP	good manufacturing practice
HACCP	hazard analysis and critical control points
HPLC	high-performance liquid chromatograph
HVAC	heating, ventilation and air conditioning
ID	identity
IR	infrared spectrophotometer
IPC	In process control
IQ	installation qualification
KF	Karl Fisher
LAF	laminar air flow
LIMS	laboratory information management system
LoD	limit of detection
LOD	loss on drying
M	meter
MB	microbiology
MBL	microbiology laboratory
MF	master formulae
MR	management review
NIR	near-infrared spectroscopy
NMR	nuclear magnetic resonance spectroscopy
NRA	national regulatory agency
OQ	operational qualification
Ph. Eur	European Pharmacopoeia

PHA	preliminary hazard analysis
PM	preventive maintenance
Ppk	process performance index
PQ	performance qualification
PQR	product quality review
PQS	pharmaceutical quality system
PRC	product release certificate
PW	purified water
QA	quality assurance
QC	quality control
QCL	quality control laboratory
QMS	quality management system
QRM	quality risk management
RA	risk assessment
RABS	restricted access barrier system
RCA	root cause analysis
RH	relative humidity
RM	raw materials
RS	reference standard
SAP	system applications products for data processing
SFG	semi-finished goods
SMS	short message service
SOP	standard operating procedure
STP	standard test procedure
T	temperature
TAMC	total aerobic microbial count
TFC	total fungal count
TLC	thin layer chromatography
TMC	total microbial count
TOC	total organic carbon
ToT	transfer of technology
UPS	uninterruptible power supply
URS	user requirements specifications
USP	United States Pharmacopeia
UV	ultraviolet-visible spectrophotometer
VMP	Validation Master Plan
WFI	water for injections
WS	working standard

Part 2	Brief summary of the findings and comments

1. Pharmaceutical quality system (PQS)

Principle

Production and control operations were specified in written form and GMP requirements were essentially being met. Managerial responsibilities were specified in written job-descriptions. Product and processes were monitored, and the results considered during batch release; regular monitoring and reviews of the quality of pharmaceutical products were being conducted according to documented schedules and procedures.

The company established the quality management system as per the requirement of the State Good Manufacturing Practices and WHO GMP. The Factory Quality Management Department and Quality Control Department were independent of the Manufacturing Department.

Management review (MR)

SOP "Quality management system review" was briefly discussed. According to the procedure MR was performed every three months (hosted by QA Manager) and annually (hosted by Vice Manager Quality). Standard agenda was specified. Minutes of MR - September 2018 were briefly discussed. During inspection, the last quarter/annual MR minutes were under preparation.

Quality Risk Management (QRM)

SOP "Quality Risk Management" described the approach to ensure the product safety and effectiveness through the life cycle. FMEA was the tool that was used to perform risk assessments.

Discussed the register for 2018 and a number of risk assessments performed.

Product Quality Review (PQR)

SOP "Annual Product Quality Revie Management" was briefly discussed and covered the product annual review process.

The PQR for XX Powder for Injection was briefly discussed. There had been no production of WHO product and the PQR consisted of a review of stability studies, HVAC, water and environmental monitoring.

The PQR for YY Powder for Injection was briefly discussed. There had been no production of WHO product and the PQR consisted of a review of stability studies, HVAC, water and environmental monitoring.

Deviations/incidents and Corrective actions and Preventive action (CAPA)

Deviations were reported, investigated and recorded according to SOP "Deviation management procedure". CAPAs were handled as per SOP "CAPA management".

The tools used for root cause analysis were as follows:
- FMEA
- 5 Whys
- Checklist
- Fishbone

Discussed the deviation log sheet for 2018 which were categorized as follows:
- Critical deviations
- Major deviations
- Minor deviations

Discussed deviation No. XX. An appropriate level of root cause analysis was applied during the investigation. The most likely root cause was identified, and the appropriate corrective and preventive actions were identified and taken.

Change control (CC)

SOP "Change Control Management", its flow chart and register for 2018, workshop 201 were briefly discussed. Changes were specified as:
- Critical
- Major
- Minor

Change Log Sheet for 2018 was briefly discussed. A number of major CCs were briefly discussed.

Data integrity

The following SOPs were briefly discussed:
- "Computer system management".
- "Data integrity management" - SOP explained ALCOA and ALCOA+ principles.
- "Empower 3 Chromatography Workstation System Management". There were 5 access levels specified Audit review register was presented to the inspectors.
- "Data backup/recovery and archival/retrieval management". Automatic back up was done daily and manual back up was done monthly. Back-ups and restored data registers were presented to inspectors.
- "Business continuity and disaster recovery plan management".

Inspectors requested company to export to Excel sheets, system and project audit trials for WHO products. Presented audit trials were reviewed and no data integrity issues noted.

Complaints

SOP "Customer complaint management", its flow chart and register for 2018 were briefly discussed. Complaints were classified as: Class I, II, III and IV.

Product returns
SOP "Management of products returns" and its flow chart and register were briefly discussed. This SOP was applicable for all products, including sterile products.

Personnel
Responsible personnel had their specific duties recorded in written job descriptions. Discussed the job description for the "Vice Manager of Quality Management Department".

2. Documentation system
Documentation system was generally established. Documents related to the manufacture of intermediates and finished products 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.

The requirements for good documentation practices were specified in SOP "Record control management procedure".

Batch release
SOP "Release management procedure" and its flow chart and SOP "Inspection records and inspection reports management" were briefly discussed. Check lists were used for BMR/BPR and analytical and microbiological test records were discussed.

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

Production of Powder for Injection XX and Powder for Injection YY was carried out in restricted access barrier system (RABS).

Inspectors observed filling line set up/assembly of equipment:
- Operator who assisted with the line set up (transferred sterilized machine parts to second operator) was standing in Grade B room.
- Second operator who performed the line set up/assembly was standing in a "contained" LAF area separated from the Grade B room by PE curtains. The RABS doors were open to Grade A "at rest", Grade B "in operation".
- Third operator who assisted with the line setup/assembly was standing in the Grade B room.

Filling
- Start up: Fill weight performed on X samples.
- In process: Fill weight performed every X minutes on Y samples.
  Note: The fill weight was determined:
  - Target fill volume
  - Alarm fill limit
  - Release fill limit

Vial integrity
SOP "Leak detection" was briefly discussed. Vial leak test was performed using 10 % Methylene blue solution.

Visual inspection
The SOPs used for the manual visual inspection were as follows:
- "201Workshop Lamp Inspection and Comparative Test SOP"
- "Powder for Injection Production Line A Lamp Inspection Process SOP"

Operators were required to take an eye break every 45 minutes. Operators were qualified once per annum as follows.

Aseptic process validation
SOP "Process simulation for preparation for injection management" and the list of persons allowed to enter Grade A/B areas and Powder for Injection Line A of workshop 201 were discussed.

Media fill validation protocol were briefly discussed.

Time limits for the storage of equipment after cleaning and sterilization and before use were established.

Maximum garment sterilization cycle validation was in progress at the time of the inspection.

Glove integrity test
RABS glove integrity test was performed SOP "Glove Leak Detector use and maintenance SOP". The parameters were as follows:

Each batch of sterile gloves used in manufacturing were tested according to the Chinese Pharmacopoeia and Chinese Standard GB 7543. Tested the following:
- Dimensions
- Water tightness
- Tensile properties
- Sterility

Cleaning and Fumigation
Cleaning was performed per SOP "Workshop 201 Normal Production Area Cleaning SOP".

4. Facilities and equipment system

Production premises were designed to avoid the unnecessary entry of supervisory or control personnel. Grade A and B areas were designed that all operations were observed from outside. In clean areas exposed surfaces were smooth, impervious and unbroken and designed to permit the repeated application of cleaning agents and disinfectants.

Equipment were located, designed, constructed, adapted and maintained to suit the operations to be carried out.

QC laboratories were separated from production areas. The QC analytical laboratories were separate from the QC microbiology laboratories. QC laboratory premises were spacious and designed to suit the operations to be carried out in them. Sufficient space was given to avoid mix ups and cross-contamination. In the QC analytical laboratories, there was adequate and suitable storage space for samples, reference standards, solvents, reagents and records. In the QC microbiology laboratories, there was adequate space for samples, reference organisms, media, testing and records. Each laboratory was equipped with adequate instruments and equipment., including work benches and work stations.

A short visit was made to the warehouse. The warehouses were of sufficient capacity to allow the orderly storage of the various categories of materials and products with proper separation and segregation - Starting materials, packaging materials and finished products. There was a separate sampling facility for starting materials. The finished goods warehouse was a high-rise warehouse with automated loading and picking systems. The warehouses were maintained within acceptable temperature and relative humidity limits.

Water system

Purified water (PW) was generated by reverse osmosis and Water for Injection (WFI) by distillation. Trends for 2018 were checked.

Sterilization tunnel validation

Re-qualification of the sterilization tunnel was carried out annually.

Autoclave validation

Autoclave re-validation was performed annually for all loads. Three vacuum cycles were applied for porous loads sterilization. Pure steam was tested for superheat, dryness value and non-condensable gases.

Steam quality

Discussed the steam test results (Workshop 201)

Two monthly sampling (all user points) was recorded on “Pure Steam Chemistry Project Batch Test Record”.

HEPA filter integrity testing
The HEPA filters were integrity tested using DOP. HEPA filters were replaced every 2 years and hence the clean room and HVAC system was requalified. The Performance Requalification Protocol The DOP integrity test was performed in-house. The photometer calibration was performed externally.

Calibration
The calibration of the magnehelic gauges was performed by North China Pharmaceutical Company Limited. The calibration certificates and working documents of the Dwyer gauges was discussed:

5. Laboratory control system

The QC function consisted of QC Analytical and QC Microbiology departments.

Sampling of components
SOP "Packaging material sampling", type III glass vials for Parenteral injection and halogenated butyl rubber stopper for injectable sterile powder STPs were briefly discussed.

Sampling of API
Sterility samples of API was not taken on the site. The API manufacturer supplied one sample for the sterility test with the actual consignment.

The identification test for APIs was controlled using "API Management Procedure" which required QA to take the necessary identification samples during production. The identification test was then performed but the batch of finished product could not be released until the identification report for the API batch was attached to the corresponding BMR.

Testing of API
Checked the testing of API XX Batch No Y and results were within specification.

Out of specification results (OOS)
SOP "Laboratory OOS/OOT investigation management", its flow chart and register (workshop 201 for 2018) were briefly discussed. The SOP was based on MHRA OOS investigation guideline. The SOP was applicable for chemical, instrumental and microbiological tests, including sterility test.

Good chromatographic practice
The following SOPs were briefly discussed:

- "HPLC testing method". SOP explained injection sequence.
- "Chromatography integration parameter setting". SOP explained manual integration: Manual integration was allowed for related substances and impurities. Manual integration should be approved by QC manager.
- "Investigation procedure for laboratory atypical results" and atypical results register.

QC Analytical laboratory
During inspection, Powder for Injection XX Batch No. Y analytical raw data was cross checked with equipment log books, standards usage and weighing slips. No discrepancies were observed.

Reference standards
Reference standards were stored in locked refrigerators, T was controlled manually twice per day. Working standards were standardized against pharmacopoeia standards and dispensed in single use vials in "clean box¨. Expiry date assigned was 1 year from the date of standardization. Alarm system was connected to Wi-Fi which generated a text message to responsible persons.

Retention samples
Retention samples were stored in movable racks. Storage was seen to be in good order. Visual checks on retention samples was carried out annually. FPP retention samples were stored expiry date + 1 year, API for 42 months.

Stability studies
Stability chambers were connected to the on-line T and RH recording system. Printouts were checked once per year. Alarm system was connected to Wi-Fi which generated a text message to responsible persons.

QC Microbiology laboratory
Access to the microbiological laboratories was restricted to authorized personnel.

The microbiology laboratories were involved in:
- Detection, isolation, enumeration and identification (Biomerieux Vitek system for identification - Contract laboratories for strain identification) of micro-organisms.
- Testing of bacterial endotoxins in different materials (e.g. starting materials, water, finished product)
- Sterility testing

The laboratory was designed specifically to avoid cross-contamination. Hence, laboratory activities such as media and equipment preparation, enumeration of micro-organisms and handling of cultures, were segregated and equipment was dedicated. There was a dedicated autoclave for the disposal of contaminated materials.

Sterility testing
Approximately 120 batches were tested per month. The sterility testing was carried out within a barrier isolator in a Grade D environment. Entry to the clean room was via a system of airlocks and a change room where the microbiologists were required to don suitable garments.

The samples (n = 20) taken for sterility testing were representative of the batch (beginning, middle and end and after any significant intervention). The sterility test was validated for the products concerned.

Discussed the training requirements for the microbiologist performing the sterility test which required the following to be completed:

- Gowning qualification
- Operation
- Performance qualification (Knowledge and testing of 3 batches)

Culture media

There were records for the receipt and preparation of culture media. The media was prepared in-house in the Media Preparation laboratory. Purified Water (PW) was used for media preparation. The PW system had multiple drops which were testing chemically and microbiologically on a monthly rotation basis. Growth promotion testing was performed on media on every batch. Both negative and positive controls were applied to test the suitability of the culture media each time the culture media was prepared and used.

Checked the preparation and growth promotion testing of the media that was used for the sterility test which was acceptable.

Reference cultures

Reference cultures which were required for the establishment of acceptable performance of the media, for validating methods, and for verifying the suitability of test methods were obtained directly from the American Type Culture Collection (ATCC). The reference strains were sub-cultured once. The microbiologists were able to demonstrate not more than five generations (passages)/subcultures from the original reference strain.

Bacterial endotoxin testing (BET)

BET test was performed using the gel clot method.

Environmental monitoring (EM)

EM trend results for Grade “A” and Grade “B” for 2018 were checked. There were no OOS results recorded.

Contract analysis

According to the information submitted before inspection some laboratories were used for contract analysis.

Technical agreements

Contract with MB Media Irradiation Company X was briefly discussed.

6. Packaging and labelling system

During inspection packaging and labeling operations were seen for Powder for Injection XX. Labelling and packaging line were connected to the filing/capping line and was continuous operation. Roll labels were used. Line clearance procedure was in place. Labeling machine was equipped with label reader and pharma code reader.

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, ***North China Pharm Co (NCPC), located at No. 115 Hainan Road, Shijiazhuang Economic & Technological Development Zone, Hebei, 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**
https://extranet.who.int/prequal/sites/default/files/documents/TRS1010_Annex10.pdf