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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
of the FPP manufacturer

Part 1	**General information**
Manufacturers Details	
Company information	
Name of manufacturer and address	Shanghai Dahua Pharmaceutical Co 3503 Changzheng Road Changzheng Farm, Chongming County Shanghai, China GPS location: Latitude: 31.76564687051916 Longitude: 121.40976190567016
Corporate address of manufacturer	As above
Inspected site	
Address of inspected manufacturing site if different from that given above	As above
Block	N /A
Inspection details	
Dates of inspection	12 – 15 March 2018
Type of inspection	Routine
Introduction	
Brief summary of the manufacturing activities	The manufacturer was involved in manufacturing, packaging, sterilizing, labelling and testing of Levonorgestrel Implant
General information about the company and site	Company Shanghai Dahua was established in 1991. Dahua site was built in 2003. Dahua is a legal business enterprise registered with Shanghai Administration of Industry & Commerce Chongming Branch. The legal pharmaceutical manufacturing license number is HU20160096 and valid until 31 December 2020. Dahua's product Sino-implant (II) (global brand name Levoplant) was initially approved by China State Food and Drug Administration (SFDA) on 8 December1994 under the approval document number (94) WYSZ X-35. The drug registration certificate was issued on 16 Aug 2002 under registration number GYZH10970174. The renewal registration was issued on 6 September 2015 and is valid for five years until 5 September 2020. The registration number remains the

	same - GYZH10970174. Sino-implant (II) is the only product manufactured at this site. There is only one production line in the building, with no separate designation of unit/block of the manufacturing site.
History of previous inspections by national medicines regulatory authorities	**Authority** / **Date/s of inspection** Nigeria: 7-9 Nov 2017 Uganda: 25 May 2017 Colombia: 9-12 Feb 2015 WHO: 8-12 May 2015 Brazil: 7-11 Dec 2015 Malawi: 18 July 2013 Sierra Leone: 12 Jan 2013 China: 28-30 May 2013 China: 29 March 2016 China: 20 July 2016
Brief report of inspection activities undertaken	
Scope and limitations	
Areas inspected	See Part 2 below
Restrictions	N/A
Out of scope	N/A
WHO product covered by the inspection	Reproductive health implants

Abbreviations

AHU	air handling unit
ALCOA	attributable, legible, contemporaneous, original and accurate
AQL	Acceptance quality limit
API	active pharmaceutical ingredient
APQR	annual product quality review
BDL	below detection limit
BMR	batch manufacturing record
BPR	batch packaging record
CAPA	corrective actions and preventive actions
CC	change control
CFU	colony-forming unit
CoA	certificate of analysis
CpK	process capability index
DQ	design qualification
EM	environmental monitoring
FAT	factory acceptance test

FBD	fluid bed dryer
FG	finished goods
FMEA	failure modes and effects analysis
FPP	finished pharmaceutical product
FTA	fault tree analysis
FTIR	Fourier transform infrared spectrometer
GC	gas chromatograph
GMP	good manufacturing practice
HACCP	hazard analysis and critical control points
HPLC	high-performance liquid chromatograph
HVAC	heating, ventilation and air conditioning
ID	identity
IR	infrared spectrophotometer
IPC	In process control
IQ	installation qualification
KF	Karl Fisher
LAF	laminar air flow
LIMS	laboratory information management system
LoD	limit of detection
LOD	loss on drying
MB	microbiology
MBL	microbiology laboratory
MF	master formulae
MR	management review
NIR	near-infrared spectroscopy
NMR	nuclear magnetic resonance spectroscopy
NRA	national regulatory agency
OQ	operational qualification
PHA	preliminary hazard analysis
PM	preventive maintenance
PpK	process performance index
PQ	performance qualification
PQR	product quality review
PQS	pharmaceutical quality system
PW	purified water
QA	quality assurance
QC	quality control
QCL	quality control laboratory
QMS	Quality management system
QRM	quality risk management
RA	risk assessment
RCA	root cause analysis
RH	relative humidity

	RM	raw materials
	RS	reference standard
	SAP	system applications products for data processing
	SFG	semi-finished goods
	SOP	standard operating procedure
	STP	standard test procedure
	T	temperature
	TAMC	total aerobic microbial count
	TFC	total fungal count
	TLC	thin layer chromatography
	TMC	total microbial count
	TOC	Total organic carbon
	URS	user requirements specifications
	UV	ultraviolet-visible spectrophotometer
	VMP	Validation Master Plan
	WFI	water for injection
	WS	working standard

Part 2	**Brief summary of the findings and comments**

1. Pharmaceutical quality system (PQS)

Principle

Production and control operations were specified in written form and GMP requirements were generally followed. Managerial responsibilities were specified in job descriptions. Product and processes were monitored and the results taken into account at batch release; regular reviews of the quality of pharmaceutical products were conducted.

Data integrity

An SOP "Data integrity" was briefly reviewed. SOP explained paperback and electronic data management based on ALCOA principles.

Quality Risk Management

An SOP "Quality Risk Management Procedure" was briefly reviewed. SOP was applicable to all stages of manufacturing cycle, including R&D and post marketing surveillance. The following tools were used for risk assessment:

- Ishikawa diagram
- FMEA (scoring for 1 to 10 was used for RPN). FMAE was used for deviations, change controls and validation RA
- HACCP

Implant risk assessment protocol No XX was briefly reviewed.

Management review

An SOP "Summary of procedures" was briefly reviewed. MR should be performed annually. Agenda specified the following items:

- Internal and external audits
- Company policy and quality target suitability
- Customer satisfaction
- Customer feedback (complaints)
- Quality system operation standards
- CAPAs review
- CAPAs review from previous MR
- Change controls
- Supplier evaluation
- Regulator changes and implementation
- Any improvements

Last MR meeting minutes were briefly reviewed. List of participants with signatures was presented to inspectors.

Product Quality Review (PQR)

An SOP "Product quality review" was briefly reviewed. The SOP stated that in case no production was done in a given year the PQR was still required for other aspects of GMP.

Functional departments involved in the annual quality review included QA, QC, Production, Supplies and Facilities. According to the SOP PQR should be prepared for the previous year and finalized by the end of the 1st quarter following year. Data was trended.

The APQR for 2016 was briefly discussed. In the PQR graphical representation of data was done when more than 7 batches of a specification were produced, and then included historical data.
Process capability was calculated using Cpk and values were specified.

Deviations

An Deviation control" was briefly reviewed. SOP was applicable for production, QA, QC, engineering and procurement departments. Deviations should be recorded in BMRs/BPRs/analytical raw data records, and reported to the supervisor. Deviations were classified as:

- Serious – investigation should be completed within 20 working days
- Major – investigation should be completed within 10 working days
- Mild – investigation should be completed within 5 working days

No serious deviations were reported in last two years.

Corrective actions and preventive action (CAPA)

An SOP "Corrective actions and preventive actions" was briefly reviewed. SOP was applicable for OOS, deviations, complaints, self-inspections, external audits and annual quality review. CAPA register was presented to the inspectors.

Change control (CC)

An SOP "Procedure for Change Control" was briefly reviewed. The SOP was applicable to changes of major suppliers of APIs and excipients, quality standards, processes, equipment/facilities, cleaning, HVAC system, water system and computer systems which affect product quality. Changes were classified as:

- Moderate
- Main

- Major

A number of CCs were briefly reviewed.

2. Good manufacturing practices for pharmaceutical products

Manufacturing processes were defined and reviewed. Qualifications and validations discussed 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. Systems were in place for handling complaints and recalling any batch of product from sale or supply.

3. Sanitation and hygiene

The company had an SOP as the basis for its approach to personal hygiene and sanitation in its production facilities. Microbial monitoring of clean room personnel was performed as part of routine batch control.

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

4. Qualification and validation

Ethylene Oxide (EtO) sterilization validation

Annex XX to the Equipment Qualification Master Plan, said that EtO sterilization should be requalified every year. An example was briefly discussed. The initial validation was a half-cycle process. Comments were made on the number and placement of sensors for T and RH during validation studies.

Cleaning validation

Implant production line cleaning validation report was briefly reviewed. Risk analysis using FMEA was used to determine possible risk of:

- Selection of testing materials
- Rationality of sampling methods
- Selection of sampling locations
- Effectiveness of analytical methods
- Scientific evaluation of limits
- Non-contingency of validation results

HPLC method was used for analysis. Microbial limit test was also performed. Only swab method was used for validation. Swab recovery average rate was 92%.

HPLC analytical method validation was part of the cleaning validation report.

Computer system validation

There was no systematic approach to validation of computerized systems.

5. Complaints

SOP "Customer complaint handling" was briefly reviewed. QA department was responsible for dealing with complaints. Complaints were classified as:

- Mild
- Major
- Serious

No complaints were registered in 2017 and none in 2018 till the date of inspection.

6. Product recalls

SOP "Products recall" was briefly reviewed. Recalls were classified as:

- Type I – notification should be made within 24 hours
- Type II - notification should be made within 48 hours
- Type III - notification should be made within 78 hours

There were no recalls in the company's history.

7. Contract production, analysis and other activities

Production activities were not contracted out.

8. Self-inspection, quality audits and supplier audits and approval

An SOP "Self-inspection" was briefly reviewed. Self-inspection should be performed at least annually. According to the SOP conflict of interests was avoided – only individuals who have no direct responsibility for the matters to be audited shall conduct the audit. Self-inspection was carried out using department wise check lists. Deficiencies were classified as:

- High risk – major
- Medium risk – moderate
- Low risk – mild

CAPAs were proposed by inspected departments and implementation was evaluated by QA department.

Supplier audits and approval

An SOP "Suppliers Management" was briefly reviewed. SOP was applicable to suppliers of raw materials, excipients and packaging materials. Materials were defined as:

- Critical
- Non-critical

Critical materials supplier's on-site audits should be conducted every two years, desk review audit (questionnaire) should be performed annually. Approved suppliers list was presented to the inspectors.
A number of supplier's audits reports were briefly discussed.

9. Personnel

There appeared to be an adequate number of personnel qualified to perform and supervise the manufacturing and quality control. Controls were in place to prevent unauthorized people from entering production, storage and QC areas.
According to the SMF the site employed approximately 65 full time employees.

10. Training

An SOP "Training" was briefly reviewed. Training effectiveness evaluation was done verbally or by written exam multiple choice questions and open questions. Only verbal training effectiveness evaluation was applied for SOP "Data integrity".
Analyst's competency list was presented to the inspectors.

11. Personal hygiene

All personnel, prior to and during employment, had to undergo an initial health examination. Direct contact between the operator's hands and starting materials, primary packaging materials and intermediate or bulk

products was avoided. Smoking, eating, drinking, chewing, and keeping plants, food, drinks, smoking material and personal medicines was prohibited in production, laboratory and storage areas.

An SOP "Hygiene" was briefly reviewed. According to the SOP employees who have direct contact with the drug production process had an annual physical examination. General production employees had bi-annually physical examination.

An SOP "Health management" was briefly reviewed. According to the SOP operators who have direct contact with API shall have progestogen exam every 2 -3 years. Health examination included heart, liver, spleen, lung; dermatology tests as well as chest X-rays, blood analysis, including hepatitis B and intestinal pathogens checks.

12. Premises

Production areas

In general, exposed surfaces were smooth, impervious and unbroken. Changing rooms were designed as airlocks and used to provide physical separation of the different stages of changing. Changing rooms were flushed with filtered air. According to the room classification, hormone production rooms where negative to corridor and other rooms. All production area was classified as class C area, supplemented with class B work benches. T & RH and pressure differentials were controlled. Smoke studies were briefly discussed for some of the Class B cabinets. No comments were made.

Within the Class C area there was a room where cleaning of equipment was done. Also, there was a room where molds were manually cleaned. These rooms were monitored in the EM program for production.
The room for preconditioning of materials before EtO sterilization had a ceiling air inlet blocked with a SS plate. Air (not HEPA filtered) leaked through the sides and caused a black deposition on the ceiling.

Ancillary areas

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

Quality control areas

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

Microbiological laboratory was separate from chemical laboratory.

13. Equipment

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

Water system

During inspection PW and WFI system was inspected. The system looked well laid out and well maintained. PW was produced using 2 RO, WFI using 4 distillation columns. Temperature, conductivity TOC and water flow were monitored / controlled on-line. PW had 2 circulation loops; one loop supplied water to the production, second to distillation columns. WFI circulation T was 80 °C. Water system was well maintained.

14. Materials

Materials were received, sampled and tested according to written procedures. Starting materials, packaging materials and finished product warehouses were inspected. Starting materials and primary packaging materials were sampled in controlled environment. Quarantine, released and rejected starting materials storage places were clearly indicated. Separate locked rooms were provided for returned/recalled goods and rejected goods.

Warehouses were outside the production building. Gowning was required for all rooms where product was stored, even for finished product in secondary packaging and for packaging materials.

15. Documentation

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

An SOP "Standard of management Procedure for Documentation" was briefly reviewed. According to the SOP records related to APIs and excipients shall be stored for at least one year after the expiry date of finished products. Documents were reviewed every 2 – 3 years. Documents were archived in closed cabinets in a room on the 3rd floor.

An SOP "Finished products release" was briefly discussed. This SOP was applicable only for finished product release. Analytical raw data was reviewed by QC manager and before release by QP. A similar procedure was applicable for API and excipients.

An SOP "Product Quality Review" - there was an original Chinese version that was authorized, and a translation in English. One signature was of the person whose function was QP/QA VP. However, the organogram showed no such function. It was explained by the company that the function of QA/Quality Director in the organogram should be read as QP/QA Vice President.
The list of batches currently on stability gave rise to a discussion on batch numbering systems. The company gave an overview of the different formats for batch numbers over the years. The company showed SOP which was titled "SMP for serial numbers and lot numbers of intermediate, to be packaged and finished product", but it turned out that for finished product a different SOP was applicable "SMP for defining production date, lot number and expiration of product".

Release specifications finished product

The final product was released according to one of four specifications.

16. Good practices in production

Generally production operations followed defined procedures in accordance with manufacturing and marketing authorizations. Deviations were investigated according to an approved procedure. Checks on yields and reconciliation of quantities were carried out. All production processes, except outer tube vulcanisation and medicine core vulcanisation were manual processes.
During inspection production operations were inspected.

17. Good practices in quality control

General

The QC function was independent from other departments. Adequate resources were available to ensure that all QC arrangements were carried out in a timely and orderly fashion. QC personnel had access to production areas for sampling and investigations as appropriate.

An SOP "Sampling of Materials" was briefly discussed. SOP was applicable for API, excipients, packaging materials, semi-finished materials and in-process materials sampling.

An SOP "Sampling of Finished products" was briefly discussed.

HPLC columns were stored in commercial packages.

An SOP "Standard procedure for integration" was briefly discussed. Circumstances of manual integration (MI) were specified in SOP. In case MI was required analyst had to notify QC manager and receive his approval. MI was recorded in separate log book and reflected in audit trail.

An SOP "Computer system management procedure" was briefly discussed.

Excel sheets were used for HPLC and GC test results calculations. HPLC calculations excel sheet inspected was validated.

All laboratory instruments were said to be connected to the UPS, the site had independent power generator. In case of power cut off this generator should start up within 10 minutes.

Only Pharmacopoeial reference standards were used for analysis.

Out of specification (OOS)

An "Out of specification investigations" and SOP DH-SOP-QC1-020/2 "Out of specification and out of limit results" were briefly discussed.

Stability studies

Stability studies were performed at the following conditions:

- 25 ± 2 °C, 60 ± 5 % RH
- 40 ± 2 °C, 75 ± 5 % RH
- 30 ± 2 °C, 75 ± 5 % RH

T and RH in the chambers were recorded continuously. Manual checks were done twice per day. Chambers were equipped with audio/visible/Wi-Fi/SMS alarm system. It was said that alarm system was challenged monthly. Chambers were connected to an UPS. In case of an equipment failure one chamber would be used for backup. This chamber was validated for all conditions.

Microbiological laboratory (MB)

MB was inspected during inspection, there were no activities going on. Separate rooms were provided for microbial limit tests (MLT), positive controls/master strains, media preparation, media sterilization, media incubation, endotoxin tests (LAL) and sterility test. MLT and positive controls and work with master strains was carried out under LAF. During inspection Tryptone Soya Medium Broth (TSB) preparation log book was

inspected. According to the media preparation media was sterilized for 15 minutes at 121°C as per dry media manufacturer's instructions.

Sterility test was carried out in isolator. It was said that fumigation of isolator was performed before and after sterility test using hydrogen peroxide. Environmental monitoring (settle plates) was performed during sterility test. Till inspection no sterility test failures were reported.

PART 3

Initial 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 ***Shanghai Dahua Pharmaceutical Co, located at 3503 Changzheng Road Changzheng Farm, Chongming County Shanghai, China*** WHO good manufacturing practices for pharmaceutical products.

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 used for assessing compliance

1. 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

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

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

4. WHO Good Manufacturing Practices: water for pharmaceutical use. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourth-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/

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

6. WHO guidelines on good manufacturing practices for heating, ventilation and air-conditioning systems for non-sterile pharmaceutical dosage forms. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report* Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 5
   Short name: WHO TRS No. 961, Annex 5
   http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

7. Supplementary guidelines on good manufacturing practices: validation. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report* Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4
   Short name: WHO TRS No. 937, Annex 4
   http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf?ua=1

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

9. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report*. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2
   Short name: WHO TRS No. 957, Annex 2
   http://www.who.int/medicines/publications/44threport/en/

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report* Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7
    Short name: WHO TRS No. 961, Annex 7
    http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

11. Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report* Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 9
    Short name: WHO TRS No. 961, Annex 9
    http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

12. General guidelines for the establishment maintenance and distribution of chemical reference substances. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-first Report* Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3
Short name: WHO TRS No. 943, Annex 3
http://whqlibdoc.who.int/trs/WHO_TRS_943_eng.pdf?ua=1

13. WHO good practices for pharmaceutical microbiology laboratories. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report* Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2
Short name: WHO TRS No. 961, Annex 2
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

14. WHO guidelines on quality risk management. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report* Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2
Short name: WHO TRS No. 981, Annex 2
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

15. WHO guidelines on variation to a prequalified product. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report* Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3
Short name: WHO TRS No. 981, Annex 3
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

16. WHO guidelines for drafting a site master file. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report* Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 14
Short name: WHO TRS No. 961, Annex 14
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

17. WHO Guidelines on good manufacturing practices: validation, Appendix 7: non-sterile process validation. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report* Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 3
Short name: WHO TRS No. 992, Annex 3
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

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

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

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

21. WHO good manufacturing practices for biological products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 3
Short name: WHO TRS No. 996, Annex 3
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex03.pdf

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

23. 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