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 and address	PT. Tunggal Idaman Abdi Latitude: 6.205071 Longitude: 106.874006 Phone +62214890208 and +622147865874
Inspected site	
Address of inspected manufacturing site if different from that given above	PT Tunggal Idaman Abdi Jl. Jenderal Ahmad Yani No 7, Jakarta Timur 13230, INDONESIA
Unit / block / plant number	Hormone plant No II, filling line 2
Inspection details	
Dates of inspection	18 - 22 May 2018
Type of inspection	Routine
Introduction	
Brief summary of the manufacturing activities	The main activity of PT. Tunggal Idaman Abdi is the aseptic manufacturing, packaging, labelling, testing and storage of hormonal contraceptives injections in small volume vials. Only pharmaceutical finished products (FPPs) were manufactured on site, both hormone and non-hormone FPPs.
General information about the company and site	PT. Tunggal Idaman Abdi, was founded in 1968, and is a national pharmaceutical company which manufactures reproductive healthcare products. Tunggal Idaman Abdi supplies products to both private and public sector in the domestic and overseas market. Until 2005, PT. Tunggal Idaman Abdi was producing the FDA-approved 3 monthly injectable Medroxyprogesterone acetate (MPA) contraceptive, i.e. Depo Provera®. For almost 30 years the company had a toll manufacturing agreement with UpJohn/Pharmacia/Pfizer until the company ceased its marketing activities in Indonesia; following this, the company developed their own brand Triclofem® for the domestic and export market. Since 1993, PT. Tunggal Idaman Abdi has also been manufacturing a monthly injectable (MPA and estradiol cypionate) contraceptive Cyclofem® under a manufacturing and marketing license from the Concept Foundation© / Health Concepts. The company has a collaborative partnership with Concept

<table>
<tr><td></td><td>Foundation©, a non-profit international organization, which aims to improve and enhance the quality of health for women in developing countries through better access to quality reproductive healthcare products at affordable prices.

The company also participates and supports the national family planning program by collaborating with The Indonesian National Population and Family Planning Board / BKKBN.

The company has two injectable hormone manufacturing facilities, which relates to the original facility (line) and a new constructed facility completed in 2014. There is also a non-hormone manufacturing facility. In the non-hormone facility the company manufactures oxytocin injection in glass ampoules.

Triclofem has been manufactured in the new facility on line 2 since the onset. The new facility houses two lines (1 & 2). The company is in the process of moving its old vial filling line currently used for Cyclofem® onto line 1 in the new facility. A commitment was made by the company that Triclofem® will not be produced on Line 1 until regulatory approval was given by WHO.</td></tr>
<tr><td>History</td><td>The site was inspected by WHO in February 2017.
The site was inspected by the following authorities:
<table>
<tr><th>Date</th><th>Name of competent authority</th><th>Country</th></tr>
<tr><td>6-Oct 2005</td><td>National Agency of Drugs and Foods Controls (NADFC)</td><td>Indonesia</td></tr>
<tr><td>6-8 Oct 2009</td><td>National Agency of Drugs and Foods Controls (NADFC)</td><td>Indonesia</td></tr>
<tr><td>9-10 Nov 2009</td><td>National Drug Authority of Uganda</td><td>Uganda</td></tr>
<tr><td>4-5 Mar 2010</td><td>Drug Administration and Control Authority of Ethiopia</td><td>Ethiopia</td></tr>
<tr><td>20-22 Oct 2010</td><td>National Agency of Drug and Food Control (NADFC)</td><td>Indonesia</td></tr>
<tr><td>8 Sep 2011</td><td>Pharmacy, Medicines& Poison Board of Malawi</td><td>Malawi</td></tr>
<tr><td>25 Oct 2013</td><td>Ministry of Health, Pharmacy & Poisons Board, Republic of Kenya</td><td>Kenya</td></tr>
<tr><td>18-20 Dec 2013</td><td>National Agency of Drug and Food Control (NADFC)</td><td>Indonesia</td></tr>
<tr><td>14-15 Dec 2015</td><td>National Agency of Drug and Food Control (NADFC)</td><td>Indonesia</td></tr>
<tr><td>2-4 May 2016</td><td>National Agency of Drug and Food Control (NADFC)</td><td>Indonesia</td></tr>
<tr><td>23-28 Feb 2017</td><td>WHO Prequalification Team</td><td>WHO</td></tr>
<tr><td>11-13 Oct 2017</td><td>National Agency of Drug and Food Control (NADFC)</td><td>Indonesia</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>Filling line 1</td></tr>
<tr><td>WHO product</td><td>Reproductive health suspension for injection</td></tr>
</table>

numbers covered by the inspection	

Abbreviations

AHU	air handling unit
ALCOA	attributable, legible, contemporaneous, original and accurate
API	active pharmaceutical ingredient
APQR	annual product quality review
AQL	Acceptance quality limit
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 essentially being met. Managerial responsibilities were specified in written job-descriptions. Product and processes were monitored and the results taken into account during batch release; regular monitoring and reviews of the quality of pharmaceutical products were being conducted according to documented schedules and procedures.

Management review (MR)
The SOP "Management review" was briefly discussed. According to the SOP MR should be performed 2 – 3 times per year. The procedure was implemented in July 2017. Standard MR Agenda was specified. First MR was held January 2018 and covered 2017 activities. List of MR meeting participants, minutes and final report were presented to the inspectors.

Quality Risk Management
The SOP "Quality risk management" was briefly discussed. According to the SOP risk was defined as Risk = Probability x Severity x Detectability.
Scoring was the following:

- Probability: 2, 4, 6, 8
- Detectability: 2, 4, 6, 8
- Severity: 2, 4, 6, 24

The SOP "Basic tools for quality management" was briefly discussed. SOP was implemented after the previous inspection as part of the CAPA. The following tools were specified:

- Cause and effect Diagram (Fish bone)
- FMEA
- 5 Whys
- Simple statistical process control
- Pareto Chart
- Process flow diagram
- Input-process-output diagram
- Affinity diagram
- Run Chart
- Check sheet

Mainly FMEA, Fish Bone and 5 Whys were used.

Risk assessment register was presented to the inspectors. "Risk assessment sterility aspect of XX injection manufacturing" was briefly discussed. This was a second RA with the first RA was performed in 2015. RA was performed starting from API sampling. Generally RA was well performed.

Product Quality Review (PQR)
The SOP "Product quality review" was briefly discussed. This procedure was updated after previous WHO inspection and was in line with current GMP requirements.

Process capability was calculated using Ppk:

Value of Ppk	Capability
<1	Not capable
1 – 1.32	Border line
>1.33	Capable

PQR for product XX from January – December 2017 was briefly discussed. PQR covered all batches released in 2017.

Deviations

The SOP "Handling of deviations" and its flow chart were briefly discussed. The SOP was applicable to unplanned deviations. Deviations were classified as:

- Critical
- Major
- Minor

Trending of deviations was implemented after previous WHO inspection. The register of deviations was briefly discussed.

Corrective actions and preventive action (CAPA)

The SOP "Corrective actions and preventive actions" and its flow diagram were briefly discussed. It was suggested to add measurement of effectiveness of CAPAs to the flow diagram. CAPAs were trended every 6 months. The register of CAPAs was presented to the inspectors.

Change control (CC)

SOP "Change control" and its flow chart were briefly discussed. Changes were classified:

- Major – direct impact or non-direct impact to the quality and safety of the product
- Minor – no impact to quality and safety of the products

Trending of changes was added to the procedure after previous WHO inspection. A high number of changes in 2017 were directly related to the WHO inspection. A register of Change Controls was presented to the inspectors.

A number of change controls were briefly discussed.

2. Good manufacturing practices for pharmaceutical products

Manufacturing processes were defined and briefly discussed. Qualifications and validations were seen to be 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 SOPs in place as the basis of cleaning and sanitation activities. Its approach to personal hygiene and sanitation in its production facilities was sound and the facilities in good condition. Personnel were seen to be performing their duties in a diligent manner. Microbial monitoring was performed of both facility and personnel.

4. Qualification and validation

Company approach of validation was explained in the Validation Mater Plan.

Aseptic process validation
The SOP "Performance qualifications (PQ) of media fill production hormone injection" was briefly discussed. SOP was revised after the previous WHO inspection. According to the SOP aseptic process validation should be performed every 6 months for one batch. In case of major changes media fills should be performed for 3 consecutive batches.

"Periodic performance qualification of media fill, hormone injection plant II, Line – 2" was briefly discussed. Lists of personnel that participated in Media fills dated XX and YY were presented to the inspectors. Their qualification status was checked.

Cleaning validation
Cleaning validation SOP was discussed. This describes general principles of cleaning validation. Report XX, was discussed.

Visual inspector's qualification
The SOP Qualification of Visual inspector/optical control" and "Visual inspector's qualification report" were briefly discussed. Qualification was carried out every 2 years.

SOP "Visual inspection/optical control" and SOP "Visual inspection of media fill" were briefly discussed. According to the company policy operators should be under 40 years old; with eye checks to be done annually.

SOP "Verification of filled vial visual inspection of Hormone Injection" was briefly discussed. This procedure was used to inspect good vials after visual inspection done by operators. Visual inspection was verified by qualified QA personnel according AQL, inspection level II.

Temperature mapping
SOP "Temperature and relative humidity mapping" was briefly discussed. Mapping was performed based on dry and rainy season. According to the SOP mapping should be repeated every three years or after any major changes.

Temperature mapping protocol/report XX "Temperature and relative humidity mapping for warehouse" was briefly discussed. During report review attention was paid to finished goods released area. 30 T mapping was performed following WHO Guideline as CAPA implementation from the previous inspection.

Sterile gowns
"Sterile gowning shelf life" validation protocol/report No XX and "Sterile gowns hold time studies in Hormone plant 2" validation report were briefly discussed.

Settle plate exposure time validation
"Validation of sterile plate exposure time for environmental monitoring", validation report was briefly discussed.

Vial leak test validation

"Validation of vial leak testing procedure" report SOP "Operation and cleaning of capping machine Bosch" were briefly discussed. Leak test was performed using Methylene blue solution in vacuum leak tester. Study was mimicking routine production process.

Label inspection machine validation

The following SOPs were briefly discussed:

- "In process control"
- "Vials labelling using Marco-Tech type LR260 machine"
- "XX 1 ml packaging/labelling instruction"
- "Operation of smart camera Mettler Toledo Model XX"
- "Operation and cleaning of BOSCH XX & YY capping machine"

URS, IQ, OQ and PQ for Smart Camera were available and presented to the inspectors. Two cameras were installed on each machine: color camera and camera that detects: missing print, partial print, serial number unknown, different serial number, defaced, print wrong position. Cameras were equipped with audit trails. During OQ&PQ it was demonstrated that operator did not have rights to change any data.

Gowning qualification, autoclave validation, depyrogenation tunnel qualification and clean room qualification were briefly discussed during previous WHO inspection.

5. Complaints

The SOP "Product complaint" and its flow chart were briefly discussed. Complaints were classified regarding product quality:

- Critical
- Major
- Minor

A numb of complaints investigation records were briefly discussed.

6. Product recalls

Recalls were classified as per National Agency of Drug and food Control guidelines:

- Class I - recall within 24 hours
- Class II – recall within 5 days
- Class III – recall within 7 days

The QA manager was responsible for dealing with recalls. The Head of Manufacturing and Plant had overall responsibility for dealing with recalls.

Up to the date of inspection there were no product recalls.

7. Contract production, analysis and other activities

Hormone tablets manufacturing operations were contracted out. The company explained that in future they were planning to manufacture hormone tablets on site.

Some laboratory tests for API attributes were contracted out. A technical agreement between XX and Tunggal was briefly discussed. The contract giver and contract acceptor rights and responsibilities were defined.

8. Self-inspection, quality audits and suppliers' audits and approval

The SOP "Self-inspection" was briefly discussed. Inspection was carried out by a self-inspection team of selected individuals drawn from relevant disciplines. Conflicts of interest were effectively avoided. Inspection was carried out at least annually for all departments. Schedule for 2017 and 2018 and lists of internal auditors were presented to the inspectors. Inspection could be carried out also unannounced.

Self-inspection of QA department inspection report was briefly discussed. Inspection report was written by the team and CAPAs addressed by the inspected department. CAPAs were tracked every month in the CAPA tracking (Excel) program.

Suppliers' audits and approval:

The SOP "Supplier qualification system" and its flow chart were briefly discussed. Suppliers audit program for 2018 was presented to the inspectors.

9. Personnel

There appeared to be an adequate number of personnel qualified to perform and supervise the manufacturing and quality control.

10. Training

Training was provided in accordance with a written training program and documented.
The SOP "Training" and training program 2018 were briefly discussed. The following trainings were listed:

- Basic GMP (presented as power point training)
- On job training
- Additional training (SOPs, refreshment and remedial (CAPA) training)
- External training

QA department training on topic "Document control and document fill in" was briefly discussed.

The SOP "Analyst qualification" was briefly discussed. Analyst qualification was performed for new analysts/new tests.

11. Personal hygiene

All personnel, prior to and during employment, had to undergo an initial health examination. Thereafter regular health examinations were carried out every year. Personnel conducting visual inspections had to undergo periodic eye examinations. 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, drink; smoking material and personal medicines was prohibited in production, laboratory and storage areas.

12. Premises

Ancillary areas

Rest and refreshment rooms were appropriately separated from manufacturing and control areas.

Production areas

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. Premises were cleaned and disinfected according to written procedures.

The new production areas were constructed to a high standard and all were seen to be properly maintained.

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.

The space constraints seen at the previous inspection had been essentially resolved except for the microbiology lab. The move of the microbiology QC activity into the new locations awaits the completion of the old filling line to the space in the new building designated as line 1. Because of delays in the validation of the new facility and increased domestic demand for product the removal of this line has taken longer than originally envisaged.

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.

Performance of HVAC system was continuously monitored by building automated system (BAS).

The SOP “Back-up of laboratory instruments electronic data” was briefly discussed.

Mitigation of disaster management was carried out after previous inspection.

As a CAPA after the previous WHO inspection a back-up portable particle counter was installed. The qualification documentation vendor was briefly discussed.

Arrangements for mitigation of power failures were briefly discussed.

Preventive maintenance

SOP “Preventive maintenance” was briefly discussed. This described preventive and corrective maintenance procedures. Annual plans were shown for a large number of categories of equipment.

14. Materials

Materials were received, sampled and tested according to relevant written procedures. Primary packaging materials were sampled in sampling room under LAF. Quarantine and release materials were appropriately labelled. Separate room was provided for storage of rejected materials. An approved suppliers list was presented to inspectors and was available in the warehouse.

Returned products

The SOP "Returned products", process flow and rejected product register were briefly discussed. SOP was applicable to all products manufactured on site.

15. Documentation

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

The Batch Manufacturing Record for batch XX was briefly discussed. In general the layout was clear and the entries made into the record were clearly legible. Dispensing of the active substance in the Class A/B area was well documented, with the responsible pharmacist countersigning weights and calculations.
The BMR contained forms in which the inspection hours and eye rest periods for visual inspectors were recorded.

16. Good practices in production

In general production operations followed defined procedures. Deviations from procedures were recorded and investigated. Access to production premises was restricted to authorized personnel.

There were 5 secondary packaging lines, four of those were used for vials labelling and packaging. Secondary packaging rooms adequately segregated.

17. Good practices in quality control

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

During inspection analysts demonstrated performance of re-suspendability and syringeability tests.

The SOP "User level of HPLC system Empower" was briefly discussed.

Analytical raw data for XX batch YY was briefly discussed.

The SOP "Sampling for starting material of hormone injectable products" was briefly discussed. Excel sheets used for calculations were validated. Audit trails were evaluated for every batch before release according check list.

Protocol/report "Verification protocol for computerized system" was briefly discussed. This document was related to excel sheets calculations verification. Protocol/report was cross checked with raw data.

Samples for identity tests of each bag of sterile API were taken during production. For other tests sampling was done according to the SOP "Raw material sampling for hormone injectable products".

Out of specification results (OOS)
In 2017 the total number of OOS was XX, which is much higher than the years before as a result of better analyst awareness after a comment was made in the previous inspection report. OOS in IPC tests were not included at the time, but rather treated as deviations. For 2017 a trend report was made for OOSs which broke down the number of OOS into 5 categories.
The SOP "Out of specifications for chemical tests" was discussed. Changes to this SOP were made after the last WHO inspection. OOS procedure was based on MHRA guidance.

A number of OOS investigation reports were discussed.

Environmental monitoring of clean area, monitoring of PW and WFI, reference materials, stability studies, retention samples and microbiology laboratory were inspected during previous WHO inspection.

PART 3
Conclusion
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, PT. Tunggal Idaman Abdi Hormone plant No II, filling line 2, located at JI. Jend. A.Yani no. 7, Jakarta, 13230, Indonesia was considered to be operating at an acceptable level of compliance with 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 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

2. 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

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. 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/

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 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

18. 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

19. 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

20. 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