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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	PT. Tunggal Idaman Abdi Latitude: 6.205071 Longitude: 106.874006 Phone +62214890208 and +622147865874
Corporate address of manufacturer	N/A
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
Manufacturing license number	License, No HK.07.IF/V/190/13, issued April 11, 2013 covering the activities of aseptic manufacturing, packaging, labeling, testing and storage of small volume injection of sex hormone and contraceptives. The GMP certificate for the manufacture of Hormone Injection pharmaceutical products in Hormone Plant-2 No 4146/CPOB/A/IV/14, issued 14 April, 2014 by the National Agency of Drug and Food Control (NAFDC/BPOM)
Inspection details	
Dates of inspection	23 - 28 February 2017
Type of inspection	Routine
Introduction	
Brief summary of the manufacturing activities	The main activity of PT. Tunggal Idaman Abdi was the aseptic manufacturing, packaging, labelling, testing and storage of small volume injections in vials of hormonal contraceptives. Only pharmaceutical finished products (FPPs) were manufactured on the site, both hormone and non-hormone FPPs.
General information about the company and	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

site

overseas market.

Until 2005, PT. Tunggal Idaman Abdi was producing the FDA-approved 3 monthly injectable Medroxyprogesterone acetate (MPA) contraceptive, namely 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; afterwards the company developed their own brand Triclofem ® for the domestic market 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 have a successful collaborative partnership with Concept 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, its original line and a newly constructed facility certified 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 outset and this new facility houses two lines (1 & 2). The company is in the process of moving its old vial filling line currently used for Cyclofem® into the line 1 space in the new facility.

History

The site was inspected by WHO in November 2014. This was pre-submission gap finding inspection specifically for MPA injection. The company submitted its dossier for Triclofem® in early 2017 and the current inspection is a routine post submission GMP assessment.

The site was inspected by the following authorities:

Date	Name of competent authority	Country
6-Oct 2005	National Agency of Drugs and Foods Controls (NADFC)	Indonesia
6-8 Oct 2009	National Agency of Drugs and Foods Controls (NADFC)	Indonesia
9-10 Nov 2009	National Drug Authority of Uganda	Uganda
4-5 Mar 2010	Drug Administration and Control Authority of Ethiopia	Ethiopia
20-22 Oct 2010	National Agency of Drug and Food Control (NADFC)	Indonesia
8 Sep 2011	Pharmacy, Medicines& Poison Board of Malawi	Malawi
25 Oct 2013	Ministry of Health, Pharmacy & Poisons Board, Republic of Kenya	Kenya
18-20 Dec 2013	National Agency of Drug and Food Control (NADFC)	Indonesia

Brief report of inspection activities undertaken	
Scope and limitations	
Areas inspected	See Part two below
Restrictions	N/A
Out of scope	*Filling line I, currently still used for the production of Cyclofem®*
WHO product numbers covered by the inspection	*RH014 Medroxyprogesterone acetate (MPA) Suspension for injection 150mg/ml (Triclofem®)*

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 (where applicable)

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 appropriately 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.

Quality Risk Management

The SOP "Quality risk management" was reviewed. This SOP utilises a risk assessment tool similar to failure modes and effects analysis (FMEA), and this methodology was the only tool used for risk assessment. In this process risk was defined as Risk = Probability x Severity x Detectability.

The following discrete steps were performed during the risk assessment:

- Risk identification
- Existing controls
- Risk evaluation
- Measures to be taken
- Risk acceptable/not acceptable

Risk assessment XX and YY were reviewed and discussed with company personnel. Generally RAs were well performed, however the limiting of assessment to a single tool based upon FMEA is undesirable as other tools may be more useful in some assessments.

The use of the FMEA like tool was in line with the NADFC/BPOM model written procedure.

Risk registers were prepared on an annual basis.

Product Quality Review (PQR)

The SOP "Product quality review" was reviewed.

Process capability was calculated using Cpk:

Value of Cpk	Capability
<1	Poor
1 – 1.32	Border line
>1.33	Capable

PQR (Triclofem®) from January 2016 – December 2016 was reviewed.

Deviations

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

- Critical
- Major
- Minor

Ishikawa diagram and 5 Why`s were used for root cause analysis.

The deviation register for 2016 was presented to the inspectors.

Deviation XX was reviewed.

Corrective actions and preventive action (CAPA)

The SOP "Corrective actions and preventive actions" and its flow diagram were reviewed. CAPAs were proposed by manager or supervisor of each department. The QA manager was responsible for reviewing and approving CAPAs. CAPAs registers were month wise.

Change control (CC)

The SOP "Change control" and its flow chart were reviewed.

Changes were classified:

- Major
- Minor

Change control XX and related autoclave performance qualification record YY were reviewed. CC was classified as major.

2. Good manufacturing practices for pharmaceutical products

Manufacturing processes were generally well defined and reviewed. Qualifications and validations were performed where necessary and the work performed of a good general standard. Significant deviations were recorded and investigated in a timely fashion, root causes were determined and CAPAs were implemented. Systems were in place for tracking these activities and these were generally sound.

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 (VMP). VMP was reviewed by inspectors. VMP was reviewed by the company twice per year. Validation schedule was presented and reviewed by inspectors. The VMP was satisfactory other than it did not address computer system validation (CSV).

Aseptic process validation

The SOP "Performance qualifications (PQ) of media fill, production hormone injection" was reviewed. 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. The media fill procedure and protocols are of a good overall standard.

"Periodic performance qualification of media fill, hormone injection plant II, Line – 2" No XX was reviewed.

This study was done before commercial production was started. There were no positives identified and the number of vials filled was sufficient to cover the shift patterns involved and the demanded interventions needed.

Gowning qualification

The SOP "Gowning procedure for grade A and B" and "Gowning qualification for grade B" report XX were reviewed. Gowning re-qualification was performed every two years.

Visual inspector's qualification

The SOP "Visual inspection/optical control" and SOP "Qualification of Visual inspector /optical control" were reviewed.

The "Visual operators qualification report (PQR)" XX was reviewed. Operators had to pass qualification exams 6 times with 100% test result in one day.

Autoclave validation

Autoclave performance qualification record XX was reviewed. This was generally satisfactory however a major issue was identified in that inadequate attention had been given to the integrity testing of the vacuum break filters of this sterilizer.

Depyrogenation tunnel qualification

Depyrogenation oven PQ report XX, PQ report YY and the SOP "Washing and sterilisation of vials using Bosch XX" were reviewed.

Qualification was carried out for both vial sizes, the following tests were performed:
- Air velocity
- Air flow pattern
- HEPA integrity
- Particle counts
- Heat penetration
- Endotoxin after depyrogenation

Generally the depyrogenation oven PQ had been carried out satisfactorily.

Clean room qualification
The air to the vial filing room was supplied by the AHU XX. Performance qualification report YY "at rest" and "in operation" were reviewed. The following tests were carried out:
- Air flow/air changes per hour
- Air flow pattern
- Pressure differentials
- Temperature and RH
- Microbial counts
- Particulate counts
- Recovery tests
- HEPA filters integrity

HVAC system was equipped by alarm, which was said to be challenged.

The filling room HVAC and clean air supply has been designed and constructed using plenum rather than ducted air supply as is common for example in US facilities but less common in other parts of the world. This approach provided challenges for the measurement and confirmation of upstream Poly Alpha Olefin (PAO) concentrations during HEPA filter integrity verifications due to dilution effects. Changes to the testing approach were recommended.

Temperature mapping
The SOP "Temperature and relative humidity mapping" was reviewed. Mapping was performed based on dry and rainy season.

Temperature mapping report "Temperature and relative humidity mapping for warehouse" XX was reviewed. During report review attention was paid to finished goods quarantine area YY.

5. Complaints
The SOP "Product complaint" and its flow chart were reviewed. Complaints were classified regarding product quality:
- Critical
- Major
- Minor

The complaints register for 2016 was presented to the inspectors.

Complaint No XX was reviewed.

6. Product recalls

The SOP "Product recall" and its flow chart were reviewed. 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. 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 currently has a project to bring these in-house.

Some laboratory tests for API attributes were also contracted out. A technical agreement was in place with XX and Tunggal was reviewed. 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 reviewed. Inspection was carried out by a self-inspection team of selected individuals drawn from relevant disciplines.

Inspection report was written by the team and CAPAs addressed by the inspected department. CAPA was tracked in the CAPA program.

According to the SOP self-inspection of all departments should be carried out once per year. Self-inspection schedule for 2016 was presented to the inspectors and was satisfactory.

<u>Suppliers' audits and approval:</u>

The SOP "Supplier qualification system" and its flow chart were reviewed. Primary packaging materials manufacturers were qualified based on:

- Questionnaire (mandatory)
- Audit (desirable)
- Samples (mandatory)

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.

Number of employees:

Processing (Non Hormone)	12
Packaging (Non Hormone)	44
Processing (Hormone)	65
Packaging (Hormone)	73
QC (shared)	26
QA (shared)	18
Plant Management	2
Product Development	4
Production Planning and Inventory Control -Warehouse (shared)	14
Plant Engineering (shared)	23
Regulatory Affairs	4
Total	285

10. Training

Training was provided in accordance with a written training program and documented.

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.

It was noted that the company had a new document control area which is significant improvement on the situation seen at the previous inspection. Nonetheless the company should consider the document life cycle for pivotal records for example: bio-batches, stability batches, BMRs and analytical test reports for these batches where the record retention period is much longer than normal GMP expectations.

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).

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.

15. Documentation

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

It was recommended that where more than a single batch of vials and or stoppers are used in manufacture of one FPP batch, that the approximate time of introduction of the new batches onto the line is recorded as to facilitate investigations should a vial or stopper related issue arise.

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.

The SOP "Operational and cleaning capping machine Bosch XX" was reviewed. Vials integrity test was performed at the beginning, middle and end of the capping process.

The aseptic vial filling line 2 was currently only used for manufacture of 2 similar products, DMPA Injection 150 mg/ml and DMPA Injection 150 mg/3ml.

There will be dedicated tank, tubing and parts for a monthly injectable (MPA + Estradiol cypionate) contraceptive Cyclofem®.manufactured on this line

During inspection it was noted that the new visual/optical control stations were in process of installation. Light intensity for visual/optical control stations was specified. Light intensity was checked once per month. During visual/optical control vials with defects were separated as per defects in locked rejected vials boxes.

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

The SOP "Vials packaging" was spot checked. Labels/information on labels was checked manually. Checks were recorded

17. Good practices in quality control

General

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.

The "User level of HPLC system Empower" was reviewed. Three user levels were specified:

- Administrator (supplier)
- Supervisor
- User

The SOP "Sampling for starting material of hormone injectable products" was spot checked.

The SOP "Visual inspection / optical control" was reviewed. Critical, major and other defects were specified based on AQL.

The SOP "Batch disposition" and its flow chart were reviewed.

Out of specification results (OOS)
The SOP "Out of specifications for chemical tests" and SOP "Out of specifications for microbial tests" were reviewed. The SOPs were applicable for investigation of OOS results of raw materials and excipients, packaging materials, APIs and finished products as well as in stability studies.

OOS register for chemical and microbial tests were presented to the inspectors

OOS investigation report XX was reviewed.

Environmental monitoring of clean area (EM)
The SOP "Environmental monitoring in production area, Hormone plant II" was reviewed and discussed. Contact plates, air samples and settle plates were used for EM.

The report of environmental monitoring No XX for period October – December 2016 was reviewed. Local flora isolates were identified and used during the media fill to confirm growth in the media fertility testing. EM monitoring of clean rooms was performed after cleaning and sanitation and before starting the operations.

The EM trends reviewed were satisfactory.

Four different cleaning agents were used in grade A and B for routine cleaning and sanitation.

Monitoring of PW and WFI
The SOP "Water quality routine monitoring in Hormone plant II" was spot reviewed. Alert limits were established 60 % from the specification. Sampling plan for WFI was in place. WFI critical sampling points were sampled and tested daily for endotoxins and microbial tests, conductivity and TOC.

Three monthly trends were performed and available for inspection PW and WFI trends October – December 2016 were reviewed.

Reference materials
The SOP "Handling of reference standards and standardisation of working standards" was reviewed.

Pharmacopoeia reference standard was used for impurity tests and working standard for assay test. Usage of reference materials were recorded in the log book.

Stability studies
The SOP "Stability study of finished product" and stability schedule for March 2017 were reviewed.

Stability chambers temperature and RH sensors were connected to the software and recorded continuously. T and RH were controlled manually twice times per day. During inspection chambers alarm system was under re-qualification.

Retention samples

The SOP "Retained samples" was reviewed. According to the SOP storage period for finished product was expiry date + 1 year and for APIs was 5 years after expiry date of API.

Microbiology laboratory

At the previous inspection the space available within QC laboratory was criticized. Subsequent to this inspection the company had moved its stability and microbiology incubators to space that previously housed the old hormone packaging area, following the transfer of packaging to the new facilities; this had considerable eased the crowding in the QC area.

The move of the microbiology laboratory to the new location had been delayed due to delays in the move of filling line I to its new location. The company has firm plans for the laboratory relocation which will resolve the issues noted in the last 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.

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-eight 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-six 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 3
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. Fifties 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. Fifties 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

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