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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Quality Control Laboratory

Part 1	**General information**		
Inspected laboratory details			
Name of Laboratory	**Bureau of Drugs and Narcotics (BDN), Ministry of Public Health, Thailand**		
Address of inspected laboratory site	Building 2, 88/7 Tiwanond Road, Muang Nonthaburi, 110 00, Thailand		
Inspection details			
Dates of inspection	16-18 September 2019		
Type of inspection	Routine inspection		
Introduction			
Brief description of testing activities	**Type of Analysis**	**Finished Products**	**Active pharmaceutical ingredients**
	Physical/Chemical analysis	Uniformity of dosage units (mass, content), pH value, water content (Karl Fischer), viscosity, loss on drying, particulate matter, disintegration, dissolution	Sulphated ash, acid insoluble ash, optical rotation, viscosity, pH value, water content (Karl Fischer), loss on drying, melting point, differential scanning calorimetry
	Identification tests	Chemical, UV-VIS, FTIR, TLC, HPLC, LC/MS, GC (FID)	Chemical, UV-VIS, FTIR, TLC, HPLC, LC/MS, GC (FID)
	Assay, impurities and related substances	HPLC, TLC, GC (FID), atomic absorption spectroscopy, UV-VIS spectrophotometry, fluorimetry, polarimetry, potentiometry	HPLC, TLC, GC (FID), atomic absorption spectroscopy, UV-VIS spectrophotometry, fluorimetry, polarimetry, potentiometry
	Microbiological analysis	Not applicable	Not applicable
	Miscellaneous	Not applicable	Not applicable

General information about the laboratory	Bureau of Drug and Narcotic, Department of Medical Sciences is responsible for – development and setting up the standard methods and services for laboratory testing in the field of pharmaceuticals and narcotics, – regulatory testing of active pharmaceutical ingredients, finished products, other materials intended for medical use, primary packaging material, – forensic analysis of narcotics, illicit drugs and psychotropic substances – managing of national pharmacopoeia – production of reference substances for utilization locally and within ASEAN member countries – managing proficiency testing programs. The Bureau is divided into 7 sections: Chemical and Physical Testing Section o Division 1 (in the inspection scope) o Division 2 (in the inspection scope) o Division 3 (in the inspection scope) Narcotic Section o Division 1 o Division 2 o Division 3 (in the inspection scope) Biological Testing Section Quality and Technical Development Section Thai Pharmacopoeia Section Reference Standard Center (in the inspection scope) Administrative Office
History	The laboratory was first inspected in May 2012 and then in November 2014. This was the third WHO PQ inspection.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	– Sample reception, identification, inventory, storage and allocation – Calibration of analytical equipment – Analytical method verification – Analytical method validation – Organizational chart – Job description – Training – Internal audits – Management review – Laboratory facilities – Water purification and distribution (chemical and microbiology analysis) – Document control – Software validation including Excel sheets

	– Test records with certificate of analysis – Data integrity, user management of chromatography software
Restrictions	None
Out of scope	None
Abbreviations	**Meaning**
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
CoA	Certificate of analysis
FPP	Finished pharmaceutical product
FTIR	Fourier transform infrared spectrophotometry or spectrophotometer
GMP	Good manufacturing practices
HPLC	High performance liquid chromatography (or high performance liquid chromatography equipment)
KF	Karl Fisher titration
LIMS	Laboratory information management system
MB	Microbiology
MR	Management review
NC	Non conformity
NCA	National control authority
NCL	National control laboratory
NRA	National regulatory agency
OOS	Out-of-specifications test result
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometry or spectrophotometer

Part 2	Summary of the findings and comments

1. Organization and Management

The Bureau of Drug and Narcotic, Department of Medical Sciences was led by the Director of the Agency. The department heads reported directly to the Director according to the reporting line indicated in the organizational chart and the job descriptions. The nomination and substitution of the key positions was assured by means of official appointment letters.

The issues noted from this section have already been addressed and will be verified during future inspections.

2. Quality management system

The quality management system was maintained by the quality manager serving also as a deputy director. The quality functions e.g. documentation system management, calibrations, internal audits, trainings were shared between the quality manager and other experienced staff, nominated by the quality manager.

Quality manual was discussed. The document was revised to conform with the General requirements for the competence of testing and calibration laboratories, ISO/IEC 17025:2017. In general, the quality manual contained the following sections:

- Quality policy
- Organization chart
- Training
- Document control system
- Control of records
- Internal audits
- Handling of complaints
- Management reviews
- Proficiency testing scheme
- Handling of out of specification
- Reference standards and reference materials

In general, the laboratory had established, implemented and maintained written SOPs as follows:

- Procedure for complaints, appeals,
- Rapid alert on product quality problems
- Management reviews
- Control of nonconforming work
- Writing standard operating procedures
- Document control
- Control of records
- Procedure for numbering system of equipment and computer hardware

- Corrective and preventive actions
- Confidentiality, impartiality and rights of the customer
- Ensuring validity/ quality of test results
- Qualification of equipment
- Etc.

Proficiency testing scheme (PTS)

Proficiency testing procedure was discussed. The procedure referenced to ISO/IEC 17043:2010 and ISO13528:2015 standards. It was noted that PT provider is Bureau of Drug and Narcotic, department of medical sciences and this procedure was applicable to various laboratories located in Thailand to take part in PT program. The BDN participated in the PTS organized by EDQM.

In addition, BDN participated in PTS provided by the USP Global Health Impact Program in 2014 (dissolution of Artemether) and 2015 (assay by HPLC for Cefalexin). The BDN also participate in the interlaboratory comparison wherein assigned value from their customers (laboratories located in ASEAN countries) were compared with BDN's analysts.

Change control system

The change control system of equipment was discussed. The procedure was limited to changes pertaining to analytical equipment and was based on the recommendation of USP 38-NF33. There was a form used for managing changes.

Deviation management

The deviations were reported to quality manager using a "note". A formal system was implemented

Out of trending (OOT)

The laboratory did not have any procedure for handling out of trend results. The procedure to be in place for the laboratory in performing trend analysis of purified water (chemical and microbiological) including but not limited to out of specifications, incidents, deviations, complaints etc.

Data integrity

The main measures of BDN to address data integrity was access control of the IT systems, audit trails (when available) and the countersigned printouts of the electronic data.

Internal audits

The internal audits were performed according to the annual program defined in SOP Internal Audits, by auditors having appropriate expertise, independent of the activity to be audited and nominated by the quality manager. The management ensure that audit observations are addressed within an appropriate and agreed timeframe.

The management review was performed at least annual. The last two management reviews covered the period of October 2017-September 2018 and October 2018-Jun 2019.

The issues noted from this section have already been addressed and will be verified during future inspections.

3. Control of documentation

Document control procedure was discussed. The procedure was written based on the ISO/IEC 17025, ISO/IEC 17043:2010 and WHO PQ GPPQCL. It was noted that quality manual and procedures were reviewed once per year. The numbering system for SOPs was described in this procedure. The procedure stated that the quality manual and SOPs should be retained for 5 years after they are obsolete. Currently, revised procedures were issued to respective department heads and obsolete copies were destroyed by the respective department heads. A separate list of external documents was maintained consisting USP, BP, Int. Ph., Ep, Thai Pharmacopoeia, Japanese Pharmacopoeia, Indian Pharmacopoeia, Merck Index, CFR, ISO 10993, BS EN455-3 etc. In place was a master list called worksheet that identifying the current version status and distribution of standard operating procedures.

The SOPs and most of the QA documents were only available in Thai language.

The issues noted from this section have already been addressed and will be verified during future inspections.

4. Records

Control of records procedure was discussed. The records were basically paper based. The test data generated electronically (e.g. by the chromatography software, Excel worksheet, etc.) were printed out. The analytical records are retained for 10 years before destruction. Records pertaining to internal/external audits, management review, records of external source, complaints and CAPA are retained for 5 years.

Control of data and information management was discussed. The procedure provided guidance on handling of electronic data including verification of raw data before final reporting. It was noted that the laboratory does not have a networking system for their chromatographic instruments and equipment. All the instruments and equipment are standalone. Backup was performed using external hard drive and USB flash drive periodically. A separate procedure require backup to be performed four times per year.

Report of analysis

The SOP for report of analysis was discussed. The procedure stated that analyst record the results and observations in the worksheet. As per paragraph 6.5, the head of the laboratory reviews the analytical report for accuracy and completeness. The head of laboratory verifies that information reported in the worksheet are correct and complete. The head of laboratory stamp the report and sign off confirming that review of the record had been completed. In addition to reviewing the analytical worksheets, the head of laboratory reviews the certificate of analysis.

The issues noted from this section have already been addressed and will be verified during future inspections.

5. Data processing equipment

Validation of spreadsheet was discussed. The procedure stated that spreadsheets should be validated during their development and periodically re-evaluated during operation. The examples of validated spreadsheets were reviewed and noted that spreadsheets were used for assay, dissolution, content uniformity, weight variation, water determination and assay by GC. The formulae were locked and cells which required input of weight, area etc. were left unlocked.

The issues noted from this section have already been addressed and will be verified during future inspections.

6. Personnel

The organizational chart of the BDN was available. Most of the personnel was permanent staff (section head and analysts) with a limited number of temporary workers (laboratory assistant) for less qualified functions (e.g. cleaning, sample movement, etc.). The personnel of the inspected areas were as follows:

- Administration: 19
- Chemical and Physical Testing Section: 44
- Narcotics Division 3: 11
- Reference Standard Center: 10

The form and content of the job descriptions was defined by the supervisory governmental body of the BDN in a booklet. The department heads, division heads, other managerial functions and their deputies were nominated by means of appointment letter. The appointment letters were circulated amongst the whole staff.

The SOP defined the general requirement of the training. The training log of an analyst were discussed. The analyst has successfully undergone competency testing of FT-IR, UV assay, HPLC assay.

The issues noted from this section have already been addressed and will be verified during future inspections.

7. Premises

The inspectors visited the physical-chemical section 2 located on level-4. The laboratory was spread over the following areas:

- Room 430, 431 Sample custodian storage room
- Room 432 Micro balance
- Room 473 UV-VIS spectrophotometer
- Room 435 Particulate test room
- Room 437 UPLC/HPLC
- Room 438 Cleaning room
- Room 403 PH meters and disintegration tester
- Room 405 Analytical balance room
- Room 647 Purified water system
- Room 505 GC room

The issues noted from this section have already been addressed and will be verified during future inspections.

8. Equipment, instruments and other devices

The BDN was equipped with the equipment, glassware and other devices required to accomplish tests in the scope of the inspection, in particular:

- Balance (micro, precision and analytical)
- pH meter
- Potentiometer
- KF titrator
- AAS
- FT-IR
- HPLC/UPLC
- HS-GC
- Dissolution tester
- Disintegration tester
- Particle size analyser
- DSC
- Auto TLC sampler and chambers,

The issues noted from this section have already been addressed and will be verified during future inspections.

9. Contracts

It was confirmed by the laboratory that there was no testing contracted to any third party laboratories.

10. Reagents

Deionized or purified water was used for preparation of reagents, buffers etc. Tap water was used to prepare deionized water. The PW was tested once per month for heavy metals and nitrates. Procedure for limit test of nitrates and heavy metals in purified water. In addition, PW was tested for microbial enumeration test once per month. The PQ was equipped with TOC and resistivity meter and results from display units were recorded once every day. The TOC and resistivity meter was calibrated by an outside party once every year.

The issues noted from this section have already been addressed and will be verified during future inspections.

11. Reference substances and reference materials

The reference materials were managed by the Reference Standard Center based on SOP and distributed to the concerned departments on demand. The reference materials received by the departments from Reference Standard Center were listed on: “List of reference standards”.

The reference materials were stored between 2-8 ^{0}C in refrigerator.

The issues noted from this section have already been addressed and will be verified during future inspections.

12. Calibration, verification of performance and qualification of equipment, instruments and other devices

The general principles of calibration and maintenance were defined in SOP Equipment calibration management. The “Programme for the preventive maintenance and calibration of equipment of BDN, Fiscal year 2019” summarized the types of instruments together with the proposed month for calibration/maintenance.

There was a working group nominated headed by the quality manager for the annual planning of the calibration/maintenance and responsible to assure the accomplishment by a contract company (preferably by the vendor).

The calibration and maintenance records of the equipment were discussed.

The issues noted from this section have already been addressed and will be verified during future inspections.

13. Traceability

The traceability of the analytical test results indicated in the CoA, the USP reference standard, the test sample, the chromatography data used for the calculations, calibration data of HPLC and GC were double checked and found appropriate.

The issues noted from this section have already been addressed and will be verified during future inspections.

14. Incoming samples

Incoming samples were received in the Sample Custody Storage (rooms 430, 431) and recorded in a sample logbook containing the following information:

- Date
- Sample internal ID
- Sample information
- Amount
- Submitted by
- Custodian
- Receiving laboratory
- Destruction information

The temperature in the Sample Custody Storage was controlled: below 27^0C. Samples requiring cold storage were stored in the refrigerator, temperature 2-8^0C.

The issues noted from this section have already been addressed and will be verified during future inspections.

15. Analytical worksheet

The details of the analytical testing were recorded in the analytical worksheets available electronically with restricted assess as fixed forms. The analytical worksheets were serving for calculations (as a calculation table) and for reporting (printed out).

The issues noted from this section have already been addressed and will be verified during future inspections.

16. Validation of analytical procedures

The analytical methods used by BDN were validated or verified, as applicable.

- Verification of Chemical Methods
- Method Validation of Chromatographic methods

As a general principle, the following methods have to be validated;

- Non-standard methods developed by the laboratory or the methods specified in the registration dossier,
- Laboratory developed/modified methods,
- Standard methods used outside their intended scope,
- Modified/amplified standard methods

The test methods of the following pharmacopoeias (as announced by the Public Health Minister) can be used upon verification:

- Thai Pharmacopoeia (TP)
- Thai Herbal Pharmacopoeia (THP)
- International Pharmacopoeia (Ph. Int.)
- United States Pharmacopeia (USP)
- British Pharmacopoeia (BP)
- British Pharmacopoeia (Veterinary)
- Other Publications recognized by the Bureau, e.g.
- European Pharmacopoeia (Ph. Eur.)
- Japanese Pharmacopoeia (JP)
- The Association of Official Analytical Chemist (AOAC)
- Thai Industrial Standard
- United Nations Recommended Methods

The method validation/verification is based on a validation protocol and the results are summarized in a report. The verification documents were discussed.

The issues noted from this section have already been addressed and will be verified during future inspections.

17. Testing

There were HPLC and GC testing on-going at the time of the inspection. For the test records discussed see Section 4, Report of analysis.

The issues noted from this section have already been addressed and will be verified during future inspections.

18. Evaluation of test results

Out of specification procedure described the procedure for investigating out of specification test results. The procedure is applicable for the quantitative analysis of active ingredients and related substances that falls outside the specifications or acceptance criteria. It was claimed that tests such as dissolution and content uniformity were out of the scope of this procedure and handled through pharmacopoeial procedure. The procedure did not state how residual test will be handled. The procedure was prepared based on the recommendation given in the USFDA, UKMHRA and OMCL guidelines.

The investigation was performed in two phases. Phase I is to determine the cause of OOS by using OOS checklist. This phase focuses on investigation of the laboratory error. Phase II investigation was conducted when the Phase I investigation cannot determine the laboratory error. The procedure provided examples of laboratory error such as instrument, reagent, reference standards, environmental condition, test methods, analysts and calculation. Retest involved analyzing a remained portion of the original sample, if original sample has been humidified or inadequate, new set of samples to be used. It was noted that laboratory does not perform sampling. The checklist used for Phase I investigation was referenced to the procedure. Phase II investigation included hypothesis for the root cause which included sonication time, freshly prepared sample etc. A second analyst retest sample in triplicate. The results from triplicate analysis were averaged and reported. The procedure was cross referenced to another procedure.

The issues noted from this section have already been addressed and will be verified during future inspections.

19. Certificate of analysis

According to the SOPs (Report of Analysis) and SOP (Control of Drug Testing Report), the results are shared with the customer on “Report of Analysis” approved by the Director. No other test records, worksheets, data is distributed for the customer.

The issues noted from this section have already been addressed and will be verified during future inspections.

20. Retained samples

Retained samples were stored in the sample custody room after testing was completed. For retained samples labeled storage at 2-8ºC, the retained samples were stored in the refrigerator. It was noted that samples were retained for 1 year if sample did not have any issues. If sample did not meet acceptance criteria, samples will be retained for 2 years.

The issues noted from this section have already been addressed and will be verified during future inspections.

21. Safety

Laboratory safety procedure was discussed which provided appropriate safety instructions for handling flammable solvents. In general, adequate safety equipment (personnel protective equipment e.g. glasses, gown, shoes, nose mask, shower, eye washer, ventilation hood) were in place.

The issues noted from this section have already been addressed and will be verified during future inspections.

Part 3	**Conclusion – Inspection outcome**

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, ***Bureau of Drug and Narcotic (BDN)***, located at ***Department of Medical Sciences, Ministry of Public Health, Nonthaburi, 11000, Thailand*** was considered to be operating at an acceptable level of compliance with WHO GPPQCL Guidelines.

All the non-compliances observed during the inspection that were listed in the full report as well as those reflected in the WHOPIR, were addressed by the laboratory, 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 5	List of WHO Guidelines referenced in the inspection report

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

2. 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

3. WHO good manufacturing practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourth-sixth Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2.
   Short name: WHO TRS No. 970, Annex 2
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/

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

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

6. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO GMP guidelines*** or ***TRS No. 986, Annex 2***
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

7. 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/

8. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 3.
Short name: WHO TRS No. 957, Annex 3
http://www.who.int/medicines/publications/44threport/en/

9. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 6.
Short name: WHO TRS No. 961, Annex 6
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

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

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

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

13. 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/

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. 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

21. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 10.
Short name: WHO TRS No. 1010, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf