20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

Prequalification Unit Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Finished Product Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	HBM Pharma s.r.o.
Corporate address of manufacturer	Sklabinska 30, Martin, 03680, Slovak Republic
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Sklabinska 30, Martin, 03680, Slovak Republic
Inspection details	
Dates of inspection	24-27 October 2022
Type of inspection	Routine GMP inspection
Introduction	
Brief description of the manufacturing activities	HBM Pharma s.r.o. is authorized to manufacture solid dosage forms as well as terminally sterilized and aseptically prepared small volume liquids.
General information about the company and site	The site was originally established in 1992 as a joint-venture of Hoechst AG Frankfurt, Germany and -Biotika a.s.. Slovenská Ľupča, Slovak Republic. In 2005 SANITAS, AB Kaunas, Lithuania became a shareholder and in 2010 the company changed its name to HBM Pharma s.r.o. The same year LIPLATS, Latvia became the main shareholder. Since 2018 HBM Pharma belongs to Grindeks, Riga, Latvia. HBM is a contract manufacturer that provides analytical and development services. The following major changes have been implemented since the last WHO inspection: New packaging lines New automated optical inspections Some changes in key personnel.
History	This was the second WHO inspection. The site is periodically inspected by the Slovak Institute for Drug Control – SIDC.

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Documents reviewed included but were not limited to: - Job descriptions for key personnel - Training - Product Quality Review - Management Review - Complaints and Recalls - Deviation control - Change Control - OOS/OOT and investigations - Validation/ Qualification/ Calibration - Sampling and testing of materials - Batch processing records - Materials Management System - HVAC System Site visited: - Manufacturing areas - QC laboratories - Stability chambers and retained samples area - Warehouses (raw materials, packaging materials, finished products)
Restrictions	The inspection focused on the manufacture of Oxytocin FPP and Magnesium Sulphate FPP
Out of scope	Products not submitted for WHO Prequalification
WHO products covered by the inspection	RH053 Oxytocin Solution for injection 10iu/mL RH063 Magnesium sulfate Solution for injection 500mg/ml (2ml) RH064 Magnesium sulfate Solution for injection 500mg/ml (10ml)
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
APS	Aseptic process simulation
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CFU	Colony-forming unit
CIP	Cleaning in place
CoA	Certificate of analysis
CpK	Process capability
DQ	Design qualification

EDI	Electronic deionization
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis
GMP	Good manufacturing practices
GPT	Growth promotion test
HEPA	High efficiency particulate air
HPLC	High performance liquid chromatography (or high performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
IQ	Installation qualification
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae
MFT	Media fill Test
MR	Management review
NC	Non conformity
NRA	National regulatory agency
OQ	Operational qualification
PHA	Process hazard analysis
PLC	Programmable logic controller
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
RO	Reverse osmosis
SIP	Sterilization in place
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer
WFI	Water for injection

Part 2	Summary of the findings and comments (where applicable)

1. Pharmaceutical quality system

A PQS was established. The company's principles, policies and objectives were detailed in the quality manual which also included the quality policy and the declaration of management's commitment for the implementation of the PQS. Additionally, it defined senior management's responsibility. Quality meetings were held quarterly, and management review meetings were organized once per year. Quality Control and Production functions and activities were independent.

Quality Risk Management

QRM was incorporated in the company's PQS and it was in line with ICH Q9 principles. A procedure providing details on conducting risk assessments was available and it took into account both internal and external parameters affecting different aspects of the PQS. It was applicable to all GMP processes ensuring the quality of the pharmaceutical products. The procedure adequately described the concepts of risk identification, risk analysis, risk evaluation, risk control, risk reduction, risk acceptance, risk communication and risk review. The preferred tool for conducting risk assessments was FMEA but other tools could also be used. The following risk assessments were reviewed:

Risk Assessment of pandemic in manufacturing activities
Risk Assessment for internal and external relevant issues.
Risk Assessment of RABS-2 line
Risk Assessment of aseptic filling of injection solutions
Risk Assessment for the preparation of injection solutions and sterilizing filtration

Product Quality Review

PQRs were conducted according to a written procedure. Different material numbers were assigned to the same product intended for different markets. PQRs were generated on a rolling basis. The plan for completion of PQRs was agreed upon with the customer (contract giver) and in case of delays, approval of the customer was necessary. The PQRs included review of the manufacturing activities, operations, and processes for which HBM was responsible according to the technical agreement. PQRs were approved by the Head of Quality Control, Head of Production and Qualified Person.

Kalceks was responsible for the final approval of the Magnesium Sulphate PQR and incorporation of the parts for which Kalceks was responsible. Similarly, Grindeks, was responsible for the final approval of the Oxytocin PQR. The following PQRs were reviewed:

Magnesium Sulphate 500mg/ml 10ml and 2ml (review period 01.10.2020 – 30.09.2021).
Magnesium Sulphate 500mg/ml 10ml and 2ml (review period 01.10.2019 – 30.09.2020).

Change Control

A formal system for change management was in place. The relevant SOP provided sufficient instructions on handling change requests and monitoring implementation and effectiveness of changes. The following changes were reviewed:

Introduction of an alternative supplier of Magnesium Sulphate API.
Change in name of the supplier of glass ampoules.
Cancellation of special cleaning process (passivation) of equipment used for Oxytocin production.
Replacement of the IMA packaging line with the Marchesini packaging line.

Deviations

There was a procedure in place for handling deviations. The head of the department where the deviation had occurred was responsible for initially classifying the deviation as critical, major, or minor. The QA department was responsible for confirming or changing the classification upon completion of the investigation by the relevant department and for monitoring CAPA implementation. Root cause investigations for major and critical deviations had to be completed within 15 days. The investigations could be extended to 30 days, if justified. Examples of deviation handling were reviewed and discussed.

2. Good manufacturing practices for pharmaceutical products

The basic principles of good manufacturing practices were generally well defined in SOPs and implemented. Manufacturing processes were adequately described and documented in BMRs and BPRs. Required resources were available, including adequate premises, equipment, and utilities as well as qualified personnel. Qualifications and validations discussed were performed according to prepared protocols. Significant deviations were documented and investigated, root causes were determined and CAPAs were implemented, where necessary.

3. Sanitation and hygiene

Premises and equipment were generally maintained at an acceptable level of cleanliness, and they were appropriately labelled. The company had procedures in place for cleaning and sanitizing solution preparation rooms as well as aseptic filling areas. Microbial monitoring of clean room personnel was performed as part of routine batch control. The gowning and changing procedures for entry into the manufacturing facilities were satisfactory and adequately described in SOPs while pictorials were affixed on the dressing rooms' walls.

4. Qualification and validation

The key principles of qualification and validation program were defined and documented in the Validation Master Plan. All working areas and facilities designed for production processes that are critical for the product quality as well as systems and manufacturing and quality control equipment, were subject to appropriate qualification and validation. Processes were validated according to written procedures and appropriate protocols and reports were available. Personnel was also qualified according to their duties and responsibilities.

Media fills

Media fills were conducted according to a written procedure. They were carried out every 6 months and the ampoule size was alternated every 6 months. The batch size for media-fills was 10% of the largest batch size manufactured on the line for the specific ampoule size. For 1ml and 2ml ampoule, the volume of the solution prepared was 50L (minimum volume that can be prepared in the mixing vessel), while for the 10ml ampoule, the volume of the solution was 100L (approximately 10% of the actual batch size). Vegetable Peptone Broth with Color Indicator was used as medium. Two batches of media fills were conducted. Different preparation vessel and storage vessel were used for each batch. The maximum holding time (30 hours) was used for the preparation and filling during media-fills. The interventions and number of interventions were defined as well as the number of personnel entering Grade B area. The following media fills were reviewed in detail:
RABS1 1ml (24.02.2021)
RABS1 10ml (19.05.2022)

Process validation

Protocols and reports were generated for processes validation which defined the critical process parameters and quality attributes that had to be assessed during the validation exercise. The following process validation protocol and report were reviewed:
Oxytocin 10IU/ml 1ml 17.04.2020 - Four consecutive batches were manufactured and evaluated.

Operator Qualification

New operators working in aseptic filling areas were qualified according to a written procedure. The procedure described in detail the training and qualification process of new operators.

Equipment Qualification

The performance Qualification of the Autoclave, including the sterilization cycle for Magnesium Sulfate were reviewed in detail. Qualification of the autoclave included the following tests:
Vacuum test
Bowie-Dick test
Empty chamber, maximum and minimum load
The Performance Qualification of the Marchesini packaging line was conducted in April 2021.

WFI Qualification-Monitoring

The WFI monitoring report was reviewed. No OOS results were registered during the review period (01.01.2021 -31.12.2021). The system was sterilized twice per year using pure steam at 121°C. Sampling points were classified as critical and less critical. Critical points were sampled every day and tested for microbiological content, TOC, and conductivity. Full chemical analysis was performed weekly. Less critical points were sampled every two weeks and some of them only if there was production.

5. Complaints

Complaints were registered and handled in accordance with a written procedure. According to the impact on patient health complaints were categorized in three classes where Class I was considered the most serious and had to be investigated within 24 hours. Since HBM acted as a contract manufacturer for Magnesium Sulphate (Kalceks) and Oxytocin (Grindeks), in most cases it assisted the contract givers in verifying the complaints and in performing root cause investigations, where relevant. Examples of complaint handling were reviewed and discussed.

6. Product recalls

HBM was the contract manufacturer for Magnesium Sulphate (Kalceks) and Oxytocin (Grindeks). According to the technical agreement, the contract givers were responsible for the release of the finished products and conducting product recalls. HBM was responsible for performing the relevant root cause investigations, where necessary.

7. Contract production, analysis and other activities

The technical agreements with the applicants of the WHO PQ products were reviewed.

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

The responsibility of qualifying API manufacturers and suppliers was defined in the technical agreement between HBM and the contract giver. Grindeks is the manufacturer of Oxytocin API and product applicant. Kalceks was responsible for the qualification of Magnesium Sulfate API and manufacturer. Excipient qualification was the responsibility of HBM.

9. Personnel

There were approximately 270 staff working on site. Production was operating in 3 shifts while Quality Assurance and Quality Control were operating in 1 shift. Organization charts were available reflecting administrative structure. Personnel were generally aware of GMP principles. There was a procedure in place for the qualification of employees which also included instructions on creating and approving job descriptions. Delegation of duties was defined in job descriptions. Job descriptions were reviewed only when changes were applicable. Job descriptions for key personnel were established and some examples were reviewed and discussed.

10. Training

There was an SOP in place providing details on the different types and areas of training including but not limited to induction and continuous training. Separate annual training plans were developed by Human Resources and Quality Assurance and more specific trainings were organized by each department. The realization of trainings was recorded. Examples of the electronic records for trainings focusing on quality activities were checked. The training material also included the questionnaire to evaluate the effectiveness of training.

11. Personal hygiene

There were procedures in place adequately defining the concepts of occupational health, hygiene, and safety. Personnel were medically examined and cleared before being employed. Thereafter periodic health examinations were carried out. Similarly, operators 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.

12. Premises

Layouts of the facilities were made available. In general, premises were designed, constructed, and maintained to suit the operations to be carried out and prevent the risk of contamination of materials and products. At large, the design of premises was such as to minimize the risk of errors and permit effective cleaning and maintenance. Premises were designed and constructed to facilitate good sanitation. Areas where sterile products were manufactured were separated from general manufacturing areas and the level of cleanliness was controlled and graded. The aseptic areas were accessed through a series of increasing cleanliness level change rooms which were supplied with clean air through HEPA filters. The production building consisted of 3 floors. Preparation of solution took place on the 1st floor. The sampling room was also located on the 1st floor as well as the dispensary. The warehouse, the cold room and the filling of ampoules area were located on the ground floor. The ampoule staging room was shared for all three filling lines. Filling of ampoules took place in two RABS lines and one isolator. Oxytocin FPP was manufactured in line 1 (RABS) and Magnesium Sulphate FPP could be manufactured in all three lines. Ampoules were collected in a common area for all three lines. For terminally sterilized products there were two autoclaves available. Aseptically filled products were transferred through a buffer chamber to the optical inspection area which consisted of three rooms. Entry to automated optical inspection was the same for material and people.

13. Equipment

The production equipment installed was of good standard and appeared to be well maintained. In general, the workflow, in the facility was appropriately designed, and the equipment appeared to

be installed to facilitate production and reduce the risk of contamination. Most of the production equipment and gauges reviewed were identified as to their content or purpose with cleanliness status identified by appropriate labels. For the RABS 1 line there were four storage tanks. Two tanks were dedicated to Oxytocin solution preparation. For the RABS 2 line there were two storage tanks. Similarly, two storage tanks were dedicated to the Isolator line.

14. Materials

Written procedures for the receipt, identification, quarantine, storage, handling, sampling, approval, or rejection of materials were checked. Material receipt operations were inspected in detail as well as management of stock. Incoming starting materials in general, followed the rules described in a written procedure. There were three approved vendor lists (API and excipients, packaging materials, services). Material labels were generated from SAP in accordance with written instructions.

15. Documentation

The documentation hierarchy was detailed in the QM, and it included three levels (Quality Manual-Quality Policy, Guidelines-Instructions-MBR, SOPs-Batch records). In general, documents were designed, prepared, reviewed, and distributed with care. Documents were regularly reviewed and kept up to date. Procedures were reviewed every 3 years.

Batch numbers were assigned according to a written procedure. Unique batch numbers were generated by SAP in a sequential order regardless of the product. It was possible to accommodate the customers batch numbers which were matched with an internal batch number generated by SAP.

16. Good practices in production

Clean rooms for the manufacture of sterile products were classified according to the expected required specifications. They were routinely monitored for particle and microbial contamination. The particle count monitoring was performed based on a procedure. In general, hygienic behavior and gowning rules in the technical areas of Grades A, B, C, were followed. There were procedures in place describing receipt of packaging materials in production. During the tour of the facilities spot-checks on BMRs of products under processing were made.

17. Good practices in quality control

Appropriate SOPs were in place for sampling and testing of PW and WFI. Additional instructions were in place for conducting off-line TOC testing. Visual inspection was conducted by qualified operators according to a written procedure. AQL level 2 was used and limits from critical, major, and minor defects were established. Visual control was performed in a dedicated room with devices of black and white background and appropriate luminosity. Operators were initially trained and qualified and then annually requalified. Appropriate passing criteria for the identification of ampoule defects were established.

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**,** ***HBM PHARMA s.r.o***. located at ***Sklabinska 30, Martin, 03680, Slovak Republic*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines.

All the non-compliances observed during the inspection that were listed in the full report as well as those reflected in the WHOPIR, were addressed by the manufacturer, to a satisfactory level, prior to the publication of the WHOPIR.

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.

Part 4	**List of WHO Guidelines referenced in the inspection report**

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eight Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO TRS No. 986, Annex 2***
   https://digicollections.net/medicinedocs/documents/s21467en/s21467en.pdf

2. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2. ***Short name: WHO TRS No. 957, Annex 2***
   untitled (digicollections.net)

3. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 3.
   Short name: WHO TRS No. 1033, Annex 3
   9789240020900-eng.pdf (who.int)

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
   https://digicollections.net/medicinedocs/documents/s21440en/s21440en.pdf

5. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty Second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8. **Short name: WHO TRS No. 1010, Annex 8**
   https://digicollections.net/medicinedocs/documents/s23455en/s23455en.pdf

6. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4.
   Short name: WHO TRS No. 937, Annex 4
   https://digicollections.net/medicinedocs/documents/s20108en/s20108en.pdf

7. WHO good practices for pharmaceutical quality control laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1.
   Short name: WHO TRS No. 961, 957), Annex 1
   https://digicollections.net/medicinedocs/documents/s18681en/s18681en.pdf

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
   https://digicollections.net/medicinedocs/documents/s22358en/s22358en.pdf

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
   https://digicollections.net/medicinedocs/documents/s19959en/s19959en.pdf

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
    https://digicollections.net/medicinedocs/documents/s18677en/s18677en.pdf

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***
    https://digicollections.net/medicinedocs/documents/s18683en/s18683en.pdf

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***
    https://digicollections.net/medicinedocs/#d/s21438en

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
    https://digicollections.net/medicinedocs/documents/s18682en/s18682en.pdf

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
    https://digicollections.net/medicinedocs/#d/s20177en/

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
https://digicollections.net/medicinedocs/#d/s20175en/

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. Good Manufacturing Practices: Guidelines on validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Third Report Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 3. ***Short name: WHO TRS No. 1019, Annex 3***
https://digicollections.net/medicinedocs/documents/s23697en/s23697en.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***
Essential Medicines and Health Products Information Portal (digicollections.net)

20. WHO Recommendations for quality requirements when plant – derived artemisin is used as a starting material in the production of antimalarial active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 6
Short name: WHO TRS No. 992, Annex 6
https://www.who.int/publications/m/item/who-recommendations-for-quality-requirements-when-plant-derived-artemisinin-is-used-as-a-starting-material-in-the-production-of-antimalarial-active-pharmaceutical-ingredients---trs-992---annex-6

21. Guideline on data integrity. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 4. ***Short name: WHO TRS No. 1033, Annex 4***
9789240020900-eng.pdf (who.int)

22. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10.
Short name: WHO TRS No. 996, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

23. 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

24. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditionning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Third Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1019), Annex 2. **Short name: WHO TRS No. 1019, Annex 2**
https://digicollections.net/medicinedocs/documents/s23699en/s23699en.pdf

25. Points to consider when including Health-Based Exposure Limits in cleaning validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 2. **Short name: WHO TRS No. 1033, Annex 2**
9789240020900-eng.pdf (who.int)

26. Points to consider for manufacturers and inspectors: environmental aspects of manufacturing for the prevention of antimicrobial resistance. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fourth Report Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 6. **Short name: WHO TRS No. 1025, Annex 6**
9789240001824-eng.pdf (who.int)

27. Production of water for injection by means other than distillation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 3. ***Short name: WHO TRS No. 1025, Annex 3***
https://www.who.int/publications-detail/978-92-4-000182-4

28. Good chromatography practice. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 4. ***Short name: WHO TRS No. 1025, Annex 4***
https://www.who.int/publications-detail/978-92-4-000182-4