World Health Organization

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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	Joint-Stock Company «Halychpharm»
Address	6/8, Opryshkivska Str., Lviv, 79024, Ukraine 49° 51'00.7"N 24° 02'28.6"E
Corporate address of manufacturer	As above
Inspected site	
Address of inspected manufacturing site if different from that given above	6/8 Opryshkivska Str., Lviv city, 79024 50/52 Promyslova Str., Lviv city, 79024 Zaklynskyh Str., Lviv city, 79024
Unit / block / plant number	Ampoule workshop, Filling area No. 2, Filling line No. 3
Inspection details	
Dates of inspection	10 - 14 December 2018
Type of inspection	Initial
Introduction	
Brief summary of the manufacturing activities	PJSC “Halychpharm” is a member company of Arterium Corporation. History: 1826 - Petro Mykolyash established a pharmacy “Under the Star” in Lviv 1900 - Established company “Petro Mykolyash and Union” 1910 - Established factory “Laokoon” 1946 - “Laokoon” renamed “Lvivpharm” 1992 - “Lvivpharm” renamed “Halychpharm”
General information about the company and site	Main activities conducted are: • Production of parenteral drugs (Large and small volume parenterals) • Production of tablets • Production of oral liquids, cutaneous solutions, solutions for external use • Production of herbal extracts. Magnesium Sulfate 50% Solution for injections is manufactured at Ampoule workshop, Filling area No. 2, Filling line No. 3.

<table>
<tr><td></td><td>Filling area No. 2 was built in 2012 and started operations on 12.12.2012.</td></tr>
<tr><td>History</td><td>This was the first WHO inspection.
The site was inspected by the following authorities:

<table>
<tr><th>Name of competent authority</th><th>Date</th></tr>
<tr><td>The State Administration of medical products of Ukraine</td><td>February 2013</td></tr>
<tr><td>The State Administration of medical products of Ukraine</td><td>February 2013</td></tr>
<tr><td>The State Administration of medical products of Ukraine</td><td>September 2013</td></tr>
<tr><td>The State Administration of medical products of Ukraine</td><td>October 2013</td></tr>
<tr><td>The State Administration of medical products of Ukraine</td><td>May 2014</td></tr>
<tr><td>The State Administration of medical products of Ukraine</td><td>April 2015</td></tr>
<tr><td>The State Administration of medical products of Ukraine</td><td>December 2015</td></tr>
<tr><td>The State Administration of medical products of Ukraine</td><td>March 2016</td></tr>
<tr><td>The State Administration of medical products of Ukraine</td><td>April 2016</td></tr>
<tr><td>The State Administration of medical products of Ukraine</td><td>May 2016</td></tr>
<tr><td>The State Administration of medical products of Ukraine</td><td>October 2016</td></tr>
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<tr><td>The State Administration of medical products of Ukraine</td><td>September 2017</td></tr>
<tr><td>The State Administration of medical products of Ukraine</td><td>March 2018</td></tr>
<tr><td>The State Administration of medical products of Ukraine</td><td>October 2018</td></tr>
<tr><td>The State Administration of medical products of Ukraine</td><td>November 2018</td></tr>
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Brief report of inspection activities undertaken	
Scope and limitations	
Areas inspected	See Part 2 below
Restrictions	N/A
Out of scope	Products out of scope of WHO PQ
WHO product numbers covered by the inspection	Magnesium Sulfate Solution for injection 500 mg/ml (10 ml)

Abbreviations

ADE	acceptable daily exposure
AHU	air handling unit
ALCOA	attributable, legible, contemporaneous, original and accurate
API	active pharmaceutical ingredient
APQR	annual product quality review
AQL	acceptance quality limit
BET	bacterial endotoxin test
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
EU	endotoxin unit
FAT	factory acceptance test
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
IFS	Information Financial System
IR	infrared spectrophotometer

IPA	isopropyl alcohol
IPC	In process control
IQ	installation qualification
KF	Karl Fisher
KPI	key performance indicators
LAF	laminar air flow
LIMS	laboratory information management system
LoD	limit of detection
LOD	loss on drying
M	meter
MB	microbiology
MBL	microbiology laboratory
MF	master formula
MR	management review
NIR	near-infrared spectroscopy
NMR	nuclear magnetic resonance spectroscopy
NRA	national regulatory agency
OQ	operational qualification
Ph. Eur	European Pharmacopoeia
PHA	preliminary hazard analysis
PM	preventive maintenance
Ppk	process performance index
PQ	performance qualification
PQR	product quality review
PQS	pharmaceutical quality system
PRC	product release certificate
PW	purified water
QA	quality assurance
QC	quality control
QCL	quality control laboratory
QMS	quality management system
QRM	quality risk management
RA	risk assessment
RABS	restricted access barrier system
RCA	root cause analysis
RH	relative humidity
RM	raw materials
RS	reference standard
SAP	system applications products for data processing
SFG	semi-finished goods
SIP	steam in place
SMS	short message service
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
UPS	uninterruptible power supply
URS	user requirements specifications
USP	United States Pharmacopoeia
UV	ultraviolet-visible spectrophotometer
VMP	Validation Master Plan
WFI	water for injections
WS	working standard

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

1. Quality system

Principle

Production and control operations were specified in written form and GMP requirements were essentially being met. Managerial responsibilities were specified in written job-descriptions. Product and processes were monitored, and the results taken into account during batch release; regular monitoring and reviews of the quality of pharmaceutical products were being conducted according to documented schedules and procedures.

Data integrity policy

Data integrity policy was briefly discussed. The policy explained the basic ALCOA principles. Training was performed for heads of department. During self-inspection deficiency was observed that not all personnel was trained on data integrity policy. CAPAs was to perform data integrity training for all departments.

Document “Back-up and restore procedure” was briefly discussed. Automatic back up was performed once per day to the separate server.

Document “Procedure of use and access to multimedia control systems with personal authentication” was briefly discussed. Three access levels were specified.

Management review (MR)

Document “Review of Pharmaceutical Quality System” was briefly discussed. According to the document, review of PQS was carried out monthly and yearly. Standard agenda was specified. Monthly PQS review from September 2018 was briefly discussed.

Quality Risk Management (QRM)

The risk management process was specified in Document "Risk Management for Quality".

Risk assessments were performed:
- To determine the frequency of scope of audits (internal and external)
- To determine the requirements for qualification and validation
- To determine process improvements periodically
- To determine risks, which can appear in case of change implementation

The tools used for risk assessments were as follows:
- Causal analysis "5 Why's"
- Cause and effect diagrams (Ishikawa diagrams)
- Failure Mode Effects Analysis - FMEA
- Fault Tree Analysis - FTA
- HACCP

Instructions which detailed the tools to be used for risk assessments were discussed:
- "Risk analysis by Fault Tree Analysis"
- "Risk identification and ranking using Ishikawa diagram"
- "Risk assessment by Hazard Analysis and Critical Control Points (HACCP)"
- "Risk assessment by Failure Modes Effects Analysis"
- "Risk identification using 5 Why"

A risk assessment for the introduction of Magnesium Sulphate Solution for Injection 500 mg/ml (2 ml and 10 ml) in Filling Room No. 2 was discussed.

Product Quality Review (PQR)

Document "Procedure for the compilation of Product Quality Review" and its flow chart was briefly discussed. PQRs were performed in accordance with a sliding schedule. The PQR schedule was presented to the inspectors.

Document "Statistical methods for performing quality reviews" was briefly discussed. Shewhart charts were used to evaluate in-process results. Calculations were done by excel sheets. Statistical calculations were carried out according to ISO 8258-2001.

PQR for Magnesium Sulfate Solution for injection 500 mg/ml (10 ml) was not available.
Therefore, as an example PQR Magnesium Sulfate Solution for injection 250 mg/ml in 5 ml and 10 ml was briefly discussed (01.10.2017 - 30.09.2018). This product was in production from 1998.

Deviations

Document "Deviation control system", its flow chart and register for 2017 - 2018 were briefly discussed. According to the SOP, deviations were classified as:
- Critical
- Major
- Minor

Excel sheets were used for deviation registration. Trend analysis was performed monthly and annually. KPIs were specified. Investigations of deviations were carried out according to the company terminology of an un-planned "self-inspection". Root cause investigations were done via self-inspection.

A number of deviations was briefly discussed.

Corrective action and preventive action (CAPA)
Document "Corrective and preventive actions" was briefly discussed. CAPA register was maintained electronically as an excel sheet.

Change control (CC)
Document "Change control", its flow chart and register for 2017 - 2018 were briefly discussed and no critical change controls were registered. The SOP was applicable to all changes including, APIs, facilities, equipment, processes, documentation etc. According to the SOP, CCs were classified as:

- Critical
- Major
- Minor

Excel sheets were used for CC registration. A number of major CC was briefly discussed.

Self-inspection
Document "Self-inspections preparation and conduction" and self-inspection schedule for 2018 was briefly discussed. Planned and un-planned self-inspections were specified and classified as level I and level II.

A level I self-inspection was carried out by head of department according to a predefined check list. A level II self-inspection was organised and carried out by a self-inspection team according to a specific defined checklist. The self-inspection team register was presented to the inspectors.

In accordance with the SOP, an un-planned level I self-inspection is carried out in case of deviations. In the event a detailed investigation had to be carried out for deviations, a level II self-inspection was carried out.

Training records of lead inspectors were briefly discussed. Self-inspectors training program ("school of auditors") and evaluation of training was also briefly discussed. After successful training, certificates were issued. Self-inspection schedule was based on risk assessment. Departmental self-inspections were carried out at least once per year.

Supplier qualification
Document "Formation of primary, scheduled and unscheduled protocol of supplier's evaluation, formation and approval of supplier's registered list, blocking suppliers" stipulated the requirements for supplier qualification.

There were three types of evaluations performed:
- Primary (new supplier)
- Scheduled (once per annum)
- Unscheduled

The scheduled evaluation of a supplier was performed according to an approved scheduled plan for the evaluation of suppliers during the previous 12 months.

An unscheduled evaluation of a supplier was conducted with every return of non-compliant material to the supplier.

The scheduled and unscheduled evaluation of suppliers was calculated based on the following criteria:
- Quality
- Statistics of supply
- Reliability of supplier

Complaints

Document "Procedure for complaints handling", its flow chart and register for 2018 were briefly discussed. The manager of non-conforming products was responsible for management of the complaints. Complaints were classified as:
- Critical
- Major
- Minor
- Not confirmed

A number of complaints and CAPAs were briefly discussed.

Product recalls

Document "Procedure for product recall" and its flow chart were briefly discussed. No product recall was recorded within the last five years. Recalls were classified as:
- Class I - Recall should be initiated within 24 hours
- Class II - Recall should be initiated within 48 hours
- Class III - Recall should be initiated within 5 days

Recall action plans were available for all markets. Effectiveness of the procedure was evaluated once per year by performing a mock recall.

Product returns

Document "Returns of products" and register were briefly discussed. Procedure was applicable for all products manufactured on site, including injections. According to the company quality policy, no re-processing or re-working was allowed.

Batch release

Document “Evaluation of batch manufacturing and batch release” was briefly discussed. Batch release was performed by the Qualified Person.

Personnel

Document “The procedure for the making of changes to the organizational structure” was reviewed. The organizational structure was presented and discussed. The organogram was part of the Quality Manual and was approved by the Executive Director and HR Director.

Document “Administration of the process of the formation and revision of regulations about the structural units and job/work descriptions” was discussed in conjunction with the job description for the “Quality Assurance and Environmental Protection and Qualified person (QP QA)” position.

The QP was required to be a professional with a higher education in pharmacy, chemistry or chemical engineering and work experience in the field of not less than 2 years in production, quality control or development of medical products. The QP QA assumed overall responsibility for the facility and the QP QC and QP R&D performed the back up of this function when delegated.

Training

The company training policy “Training and development of personnel” was presented and discussed. Personnel were trained according to document "Organization of Staff Training Process".

The training was performed in three stages:

- Initial training
- Ongoing “periodic” training
- Unplanned training

According to the document "Development and approval of training programs for personnel”, the training programs were developed by the “Authorized Specialist in Training and Staff Development” in conjunction with the departmental specialist and approved by the required personnel.

The GxP training was covered by instruction document GxP programs training for personnel”.

Personal hygiene

Health checks were performed at recruitment (basic), periodically and unscheduled, when required. The basic and periodic health checks of the employee was conducted by health care professionals in compliance with the requirements of Order No. 246 of the Ministry of Health of Ukraine of 21.05.2007.

During the basic health check (while recruiting), the initial health indicators and health status of the employee was determined. On receipt of a medical certificate, the employee was permitted to perform the required job function. If an employee was transferred, then the employee would be referred to the Medical Station for the required compulsory medical checks.

Where required, employees underwent obligatory and periodic routine drug testing. Employees for whom basic and periodic mental examinations are obligatory were required to submit a certificate in accordance with Order # 1465 of the Cabinet of Ministers of Ukraine of 27-09-2000.

Personnel in direct contact with product were required to undergo a medical examination twice a year.

Employees' medical records were kept at the Card-register room at the Medical Station.

Personnel were provided with appropriate work clothes and individual personal protective equipment (PPE), where required. The garments were prepared according to document "The procedure of preparation of personnel's clothing for production areas and quality control areas". Personal protective equipment (PPE) was according to the document "The procedure of preparation of individual safety means".

Documentation
The documentation system was generally established.

The documentation system consisted of four levels:
- Strategic - Policies
- Operational - SOPs
- Instructions
- Protocols and records

Documents related to the manufacture of intermediates and APIs were prepared, reviewed, approved and distributed according to written procedures. The SOPs were also displayed at appropriate points. The issuance, revision, superseding and withdrawal of documents were controlled with maintenance of revision histories.

2. Production system
Production operations followed defined procedures. Qualifications and validations were performed according to approved protocols. Significant deviations from the initial protocol were recorded and investigated, root causes were determined and CAPAs were implemented where necessary. Checks on yields and reconciliation of quantities were carried out. Access to production premises was restricted to authorized personnel.

3. Facilities and equipment system
During inspection, the inspectors visited the Ampoule workshop, Filling area and filling line where 6 Magnesium Sulfate Solution for injection 500 mg/ml (10 ml) submission batches were manufactured.

Manufacturing facilities seen were in good condition.

Solution preparation was carried out in grade C environment. Reactor was equipped with spay ball - WFI T of 75 °C - 80 °C for 15 minutes. After cleaning samples were taken and analyzed. If positive results obtained, then SIP was used for sterilization (121 °C for 15 minutes) of reactor. Air vent filter

was changed regularly, integrity tests were performed. Filling was done at grade A within a grade B environment. Solution before filling was filtered via 1-micron filter and via 0.22-micron filter. Filter integrity tests was performed before production and after production. Ampoule visual inspection was carried out automatically.

Ampoule sterilization tunnel and autoclave validation records were briefly discussed.

Manual visual inspection process qualification
With regards the qualification of the manual visual inspection process, the document "Procedure for qualification of medical products reviewers" was initiated and approved.

The qualification was performed by detecting and removing predefined defective ampoules in varying formats in a controlled manner.

All employees underwent an eye inspection test (near vision acuity and color blindness) prior to employment and this was repeated six-monthly.

HVAC qualification
AHU No XX serving air to the Filling line re-qualification report was briefly discussed. Re-qualification was carried out annually, HEPA filter integrity tests every 6 months.

Environmental monitoring (EM)
EM trends for Filling line and personnel monitoring trends were presented to the inspectors. Action and alert limits were based on historical data and reviewed annually.

Purified water (PW)
PW system was seen to be well maintained. PW was produced by reverse osmosis. Regeneration of carbon filter and sand filter was performed every 24 hours. Water was distributed by two continuous circulation loops. Conductivity and TOC were monitored on line. T and velocity were monitored at the return loop. PW trends were presented to the inspectors. Action and alert limits were based on historical data and reviewed annually.

Compressed air
Compressed air quality was checked every 3 months.

Cleaning validation
Cleaning validation approach was worst case approach, taking into account PDE values. Worst case product was XX. Sampling methods used was rinse and swab methods. Rinse samples were used for cleaning monitoring. Cleaning monitoring was carried out for product change over.

Hold time studies
Hold time studies were performed for all products. Magnesium Sulfate Solution for injection 500 mg/ml (10 ml) hold time studies were performed along with process validation studies.

4. Laboratory control system
The QC function consisted of QC Biology (microbiology and pharmacology testing), QC Operative and QC Analytical.

QC Biology
The Biology laboratory was separate from the production areas. Access was restricted to authorized personnel only. The laboratory activities, such as media and equipment preparation and enumeration of microorganisms was segregated.

The sterility testing was carried out in a Grade A unidirectional airflow zone located within a clean room with a Grade B background. The air supplied to the Grade A and B zones was via HEPA filters. The sterility test was validated for each of the products manufactured.

There were 2 autoclaves. There was an autoclave for the sterilization of equipment and media and a dedicated autoclave for decontamination. The autoclaves were validated for each operating cycle and load configuration used. There were sterilization records available for each sterilization run and these records were reviewed and approved.

The media was prepared in-house, Growth promotion testing was done on all media on every batch. The performance of the media was checked with regard recovery of the target organisms. In addition, pH was also checked.

Reference cultures were used for establishing acceptable performance of all media and for validating the microbiological methods used. Traceability to the international collection was demonstrated. Working stock solutions were not used for not more than five generations/passages.

The effectiveness of the disinfectants was determined. The disinfectants were monitored for microbial contamination. The disinfectants used in Grade A and B areas were sterile before use.

The bioburden of starting materials was performed. The starting material specifications included the requirements for microbiological quality.

The Bacterial Endotoxin Test (BET) and particulate contamination (sub-visible particle test) was performed in another laboratory which was housed in the same facility that housed the API materials.

Endotoxins were detected via the gel clot method in the starting materials, WFI samples and finished product.

QC Analytical Laboratory

The inspectors visited the QC Analytical Laboratory and the laboratory was of a suitable size. Glassware was handwashed. There was a laboratory for wet chemistry and instrument rooms which housed the necessary instruments. There were separate storage facilities for reagents and equipment.

Instruments qualification

"Installation of audit trail to invisible particle counting device XX" was briefly discussed. The following documents were presented to the inspectors:

- URS
- DQ
- Certificate of software validation
- Traceability matrix
- 21 CFR Part 22 compliance certificate
- Release notes
- IQ/OQ/PQ

Sampling (performed by Group of operative control)

Document "Selection order of packaging products and auxiliary materials samples" was used for the sampling of packaging materials. The ampoule sampling plan was specified in the ampoules STP. Sampling was done according to the AQL sampling level II, defects were classified as critical, major and minor and appropriate AQL levels were applied.

Retention samples

Separate SOPs were available for the storage of APIs, packaging materials and finished product retention samples. Finished products retention samples were stored for the expiry date + 1 year and APIs stored for the expiry date + 2 years.

Contract analysis

A number of contract laboratories were used for contract analysis. Contract with "XX" Ltd and laboratory audit report were briefly discussed.

5. Materials system

Inspectors visited:

- APIs warehouse located at 6/8 Opryshkivska Str., Lviv city, 79024
- Packaging materials warehouse located at 50/52 Promyslova Str., Lviv city, 79024
- Primary packaging materials warehouse located at 5 Zaklynskyh Str., Lviv city, 79024

Finished products warehouse was located at 8-A Antonova Str., Chayky village, Kiev Svyatoshinsky district; Kiev region, 08130. This warehouse was not visited during inspection.
*All warehouses are acceptable for storage: APIs, packaging materials, FPP.

Information Financial System (IFS) combined with manual system was used for materials management.

Procedures were available to explain materials transportation from different warehouses to production.

T mapping report for APIs warehouse (summer period) was presented to the inspectors. Study was done according to the WHO guideline. Winter T mapping study was in process during the inspection.

6. Packaging and labelling system

During the inspection, labelling and packaging of Magnesium Sulphate 250 mg/ml, 5 ml was carried out.

Packaging machine was equipped with pharma code reader and printed information detector. During packaging, attention was given to minimizing the risk of cross-contamination, mix ups or substitutions.

Different product packaging operations were well segregated. Steps were taken to ensure that the work area, packaging lines, printing machines and other equipment were clean and free from any products, materials or documents used previously. Line clearance was recorded.

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, ***Joint-Stock Company «Halychpharm» located at 6/8, Opryshkivska Str., Lviv, 79024, Ukraine*** 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***
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

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 GMP for APIs*** or ***TRS No. 957, Annex 2***
http://www.who.int/medicines/publications/44threport/en/

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. 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/

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
http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf?ua=1

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 GPPQCL Guidelines or ***TRS No. 957, Annex 1***
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 2
Short name: WHO TRS No. 957, Annex 2
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. 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***
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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
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