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**Prequalification Team Inspection services**
**WHO PUBLIC INSPECTION REPORT**
**of the FPP manufacturer**

| **Part 1** | **General information** |
|---|---|
| **Manufacturers Details** | |
| Company information | |
| Name of manufacturer and address | Guilin Pharmaceutical Co. Ltd.<br>No.43, Qilidian Road, Guilin, Guangxi, China, 541004<br><br>North latitude: N25º14'42.31"<br>East longitude: E110 º 20'22.58"<br>D-U-N-S: 65-426-5578 |
| Corporate address of manufacturer | As above |
| **Inspected site** | |
| Address of inspected manufacturing site if different from that given above | As above |
| Workshop | INJ-I, INJ-II, INJ-VI, Co-packaging center for Artesunate for Injection |
| Manufacturing license number | No GUI 20160059, valid till 31 December 2020, issued by Food and drug Administration of Guangxi Zhuang Minority Autonomous Region. |
| **Inspection details** | |
| Dates of inspection | 8 – 12 May 2017 |
| Type of inspection | Routine |
| **Introduction** | |
| Brief summary of the manufacturing activities | The products of the company include APIs, sterile bulks/APIs, powders for injection, small volume parenteral (SVP) injections, tablets, soft capsules, hard capsules.<br>WHO products include: Artesunate API, sterile Artesunate bulk powder (aseptic process), Artesunate powder for injection finished pharmaceutical product (aseptic process), diluent and solvent SVP (terminally sterilized). |
| General information about the company and site | Guilin Pharmaceutical Co., Ltd. is a subsidiary company affiliated to Shanghai Fosun Pharmaceutical (Group) Co., Ltd. The site inspected is located at No.43, Qilidian Road, Guilin, Guangxi, China, 541004, about 40km from the Guilin Liangjiang airport in the outskirts of the city. APIs and finished pharmaceutical |

<table>
<tr><td></td><td>products are manufactured at this site.<br>A list of production blocks and associated dosage forms is presented in the table below. Production workshops covered by this inspection are listed below:
<table>
<tr><th>Building</th><th>Corresponding production workshop</th><th>Dosage form</th></tr>
<tr><td>5</td><td>INJ I</td><td>Powder for injection</td></tr>
<tr><td>5</td><td>INJ II</td><td>Small Volume Parenteral Injection</td></tr>
<tr><td>19</td><td>INJ VI</td><td>Small Volume Parenteral Injection</td></tr>
<tr><td>20</td><td>Co-packaging center for Artesunate for Injection</td><td></td></tr>
</table></td></tr>
<tr><td>History</td><td>WHO on-site inspections are listed in the table below:
<table>
<tr><th>Date of inspection</th><th>Production workshop/ Products</th></tr>
<tr><td>2012.07</td><td>API-I & API-II</td></tr>
<tr><td>2014.07</td><td>API-I & API-II</td></tr>
<tr><td>2016.03</td><td>API-I & API-II</td></tr>
<tr><td>2012.07</td><td>OSD-I</td></tr>
<tr><td>2014.07</td><td>OSD-I</td></tr>
<tr><td>2016.03</td><td>OSD-I</td></tr>
<tr><td>2014.07</td><td>INJ-I & INJ-V and INJ-II & INJ VI (SVP)</td></tr>
<tr><td>2016.03</td><td>INJ-I and INJ-II & INJ VI (SVP)</td></tr>
</table></td></tr>
<tr><td>Brief report of inspection activities undertaken</td><td></td></tr>
<tr><td>Scope and limitations</td><td></td></tr>
<tr><td>Areas inspected</td><td>See Part 2 below</td></tr>
<tr><td>Restrictions</td><td>INJ-VI was inspected in the scope of terminally sterilised SVPs - Sodium bicarbonate and Sodium chloride.<br><br>Note: INJ-VI is also for aseptic production of SVPs not under WHO PQ.</td></tr>
<tr><td>Out of scope</td><td>N/A</td></tr>
<tr><td>WHO product numbers covered by the inspection</td><td>MA051 Artesunate for Injection+ Sodium Bicarbonate Injection + Sodium Chloride Injection - (Vial + Ampoule) ; 60mg/vial + 50mg/ml + 45mg/5ml<br>MA089 Artesunate for Injection+ Sodium Bicarbonate Injection + Sodium Chloride Injection - (Vial + Ampoule) ; 30mg/vial + 25mg/0.5ml + 22.5mg/2.5ml<br>MA090 Artesunate for Injection+ Sodium Bicarbonate Injection + Sodium Chloride Injection - (Vial + Ampoule) ; 120mg/vial + 100mg/2ml + 90mg/10ml</td></tr>
</table>

Abbreviations

| | |
|---|---|
| AHU | air handling unit |
| ALCOA | attributable, legible, contemporaneous, original and accurate |
| AQL | Acceptance quality limit |
| API | active pharmaceutical ingredient |
| APQR | annual product quality review |
| BDL | below detection limit |
| BMR | batch manufacturing record |
| BPR | batch packaging record |
| CAPA | corrective actions and preventive actions |
| CC | change control |
| CFU | colony-forming unit |
| CoA | certificate of analysis |
| CpK | process capability index |
| DQ | design qualification |
| EM | environmental monitoring |
| FAT | factory acceptance test |
| FBD | fluid bed dryer |
| FG | finished goods |
| FMEA | failure modes and effects analysis |
| FPP | finished pharmaceutical product |
| FTA | fault tree analysis |
| FTIR | Fourier transform infrared spectrometer |
| GC | gas chromatograph |
| GMP | good manufacturing practice |
| HACCP | hazard analysis and critical control points |
| HPLC | high-performance liquid chromatograph |
| HVAC | heating, ventilation and air conditioning |
| ID | identity |
| IR | infrared spectrophotometer |
| IPC | In process control |
| IQ | installation qualification |
| KF | Karl Fisher |
| LAF | laminar air flow |
| LIMS | laboratory information management system |
| LoD | limit of detection |
| LOD | loss on drying |
| MB | microbiology |
| MBL | microbiology laboratory |
| MF | master formulae |
| MR | management review |
| NIR | near-infrared spectroscopy |
| NMR | nuclear magnetic resonance spectroscopy |
| NRA | national regulatory agency |
| OQ | operational qualification |
| PHA | preliminary hazard analysis |
| PM | preventive maintenance |
| PpK | process performance index |

| | |
|---|---|
| PQ | performance qualification |
| PQR | product quality review |
| PQS | pharmaceutical quality system |
| PW | purified water |
| QA | quality assurance |
| QC | quality control |
| QCL | quality control laboratory |
| QMS | Quality management system |
| QRM | quality risk management |
| RA | risk assessment |
| RCA | root cause analysis |
| RH | relative humidity |
| RM | raw materials |
| RS | reference standard |
| SAP | system applications products for data processing |
| SFG | semi-finished goods |
| SOP | standard operating procedure |
| STP | standard test procedure |
| T | temperature |
| TAMC | total aerobic microbial count |
| TFC | total fungal count |
| TLC | thin layer chromatography |
| TMC | total microbial count |
| TOC | Total organic carbon |
| URS | user requirements specifications |
| UV | ultraviolet-visible spectrophotometer |
| VMP | Validation Master Plan |
| WFI | water for injection |
| WS | working standard |

| **Part 2** | **Brief summary of the findings and comments (where applicable)** |
|---|---|

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

## 1. Pharmaceutical quality system (PQS)

Principle

Production and control operations were specified in written form and GMP requirements were generally followed. Managerial responsibilities were specified in job descriptions. Product and processes were monitored and the results taken into account at batch release; regular reviews of the quality of pharmaceutical products were conducted.

Quality Risk Management

The SOP "Quality Risk Management" was discussed. The SOP described:

- Risk identification
- Risk analysis

- Risk evaluation
- Risk reduction
- Risk acceptance
- Risk communication
- Risk review

Failure modes and effects analysis (FMEA) was used for risk assessment. In the FMEA approach scoring from 1- 4 was used for individual elements of the Risk Priority Number (RPN) calculation.

Risk assessment (RA) for 2016 was presented to the inspectors. Formal RA was performed for Artesunate powder for injection during process validation studies.

RA "Risk assessment for modification of SVP INJ VI production line, facilities, equipment" was discussed.

Product Quality Review (PQR)

The SOP "Annual quality review of products" was discussed. The SOP stated that in case no batches were manufactured during the review period, PQR should be prepared according to the SOP. PQR reports were prepared for the period January to December. SOP contained all sections listed in the cGMP guideline.

A number of PQRs for 2016 were discussed.

Deviation and Change control registers for INJ I and INJ V were cross checked with PQRs (INJ V was operated until 2016 March).

Process capability was calculated using Cpk.

Management review (MR)

The SOP "Management review" was discussed. According to the SOP, quality system review shall be performed at least once per year. The SOP was applicable but not limited to:

- Follow-up actions from previous reviews
- Process performance and product conformity
- CAPAs
- Customer feedback and complaints
- Internal quality audits / regulatory inspections and customer audits
- Changes
- Recommendations for improvements
- OOS/OOT etc.

Deviations

The SOP "Deviation handling" and its flow chart were discussed. Deviations were classified as:

- Critical
- Major
- Minor

Deviations were trended, report for 2016 was discussed.

Root Cause Analysis

The SOP "Root cause management procedure" and its flow chart were discussed. The following tools were used to identify possible root cause:

- Ishikawa
- 5 Why's
- 5 M`s

Root cause analysis was performed by teams set up case-by-case under QA leadership.

Corrective actions and preventive action (CAPA)

The SOP "Corrective actions and preventive actions" was discussed. The SOP was applicable to:

- Complaints
- Recalls
- Deviations
- Self-inspection/ external inspection
- Process capability analysis
- OOS/OOT.

CAPAs register related to the self-inspections/external inspection and customer audits was maintained and presented to the inspectors. Other CAPAs were maintained as part of, for example, deviation and complaint investigations (described in the respective case reports).

Change control (CC)

The SOP "Change management" and its flow chart were discussed. The SOP was applicable to various GMP related changes.

Changes were classified as:

- Major - should be approved by QA manager and Head of quality
- Minor - should be approved by QA manager.

CC registers were maintained by QA.

A number of CCs were discussed.

## 2. Good manufacturing practices for pharmaceutical products

Manufacturing processes were defined and reviewed. Qualifications and validations were seen to be performed according to prepared protocols. Significant deviations from the initial protocol were recorded and investigated, root causes were determined and CAPAs were implemented where necessary. Systems were in place for handling complaints and recalling any batch of product from sale or supply.

## 3. Sanitation and hygiene

The company had an SOP as the basis for its approach to personal hygiene and sanitation in its production facilities. Microbial monitoring of clean room personnel was performed as part of routine batch control.

Generally the facilities were noted to be clean and well organized during the inspection.

## 4. Qualification and validation

Aseptic process validation

Media simulation study was discussed for INJ I and sterile Artesunate API powder/bulk. There had been no media fill positives to date. The media simulation procedure gave appropriate guidance on the actions to be taken in the event of a positive been found.

The most recent sterile Artesunate API media fill protocol XX and report YY were discussed. Media simulation was performed using sterile Tryptic Soy Broth – TSB media. The procedure required manipulation to ensure that internal surfaces were in contact with media. Containers were incubated in upturned position in two media fill incubation rooms at temperature 20- 25 ºC for (7 days) and 30 – 35 ºC (7 days).

Container-closure integrity

Container-Closure (cans) sealing integrity test protocol XX and report YY, and vials integrity test protocol ZZ and report WW were discussed.

Autoclave validation

Autoclave (used for Al flip-off caps) validation protocol XX and report YY were discussed. Validation was performed following EN285. TCs were calibrated before and after autoclave validation runs.

Dry heat sterilization oven validation

Dry heat sterilization oven (used for sterile API cans) validation protocol XX and report YY were discussed. Requalification was performed every year (heat penetration and de-pyrogenation challenge tests). HEPA filter integrity test, airborne particles, and viable particles tests were performed every 6 months. An endotoxin challenge test was performed once per year.

## 5. Complaints

The SOP “Customer complaint handling” and its flow chart were discussed. Complaints were received by complaints coordinator from the QA. Complaints were classified regarding product quality:

- Class I
- Class II
- Class III

and

- Adverse reactions
- Falsified medicines (counterfeit)

Complaints log book for 2016 was presented to the inspectors.

A number of complaints were discussed.

## 6. Product recalls

The SOP “Product recall” and its flow chart were discussed. Responsible person for making decision about recall was QA Vice-president.

Recalls were classified as per CFDA guidelines:

- 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 72 hours

**7. Contract production, analysis and other activities**

Manufacturing operations were not contracted out. Some tests were contracted out to a Governmental laboratory.

**8. Self-inspection, quality audits and supplier audits and approval**

The SOP "Self-inspection" was discussed. Inspection was carried out by a nominated self-inspection team. According to the SOP, conflict of interest should be avoided.

Inspection was carried out using a check list. Inspection report was written by the team and CAPAs addressed by the inspected department, evaluated and approved by QA. CAPA implementation was also checked by QA.

Supplier audits and approval

The SOP "Vendor audit procedure" and it's flow chart were discussed. The SOP stated that audits of manufacturers of starting materials and primary packaging materials were performed before vendor approval and subsequently every 3 years. Approved vendors lists for starting materials, excipients and packaging materials were presented to the inspectors. Approved vendors lists were updated quarterly and distributed to relevant departments. Profile folders were maintained for each supplier.

**9. Personnel**

There appeared to be an adequate number of personnel qualified to perform and supervise the manufacturing and quality control. Controls were in place to prevent unauthorized people from entering production, storage and QC areas.

**10. Training**

The SOP "GMP training", SOP "Instrumental analyst's supervisor job description" and SOP "Instrumental analyst job description" were discussed.

Analyst competency matrix was presented to the inspectors.

**11. Personal hygiene**

All personnel, prior to and during employment, had to undergo an initial health examination. Thereafter regular health examinations were carried out every year. Personnel conducting visual inspections had to undergo periodic eye examinations every six months. Direct contact between the operator's hands and starting materials, primary packaging materials and intermediate or bulk products was avoided. Smoking, eating, drinking, chewing, and keeping plants, food, drink; smoking material and personal medicines was prohibited in production, laboratory and storage areas.

**12. Premises**

Ancillary areas

Rest and refreshment rooms were separate from manufacturing and control areas.

Production areas

In general, exposed surfaces were smooth, impervious and unbroken. Changing rooms were designed as airlocks and used to provide physical separation of the different stages of changing. Changing rooms were flushed with filtered air. Premises were cleaned and disinfected according to written procedures.

Production of products under WHO PQ took place in the building called “manufacturing centre of dosage forms”; the ground floor of the building contained two production workshop for injectables:

| | |
|---|---|
| INJ I | Artesunate sterile bulk powder (in cans) and finished product (in vials) |
| INJ II | Sodium bicarbonate and Sodium chloride ampoules |

Ampoules were also produced in the adjacent separate building, on the production workshop

| | |
|---|---|
| INJ VI | Sodium bicarbonate and Sodium chloride ampoules |

Sodium bicarbonate and Sodium chloride solutions were filled under aseptic conditions because the same production workshop were also used for aseptically produced products (not under WHO PQ); the main factor was the volume of ampoules. Sodium bicarbonate and Sodium chloride ampoules were subsequently terminally sterilized.

Final packaging took place in the separate building:
Co-packaging centre Artesunate vials with Sodium bicarbonate and Sodium chloride ampoules

**INJ I and INJ II**

INJ I and INJ II were in the same building as facilities for OSDs. Different blocks had different access areas. Access to the production areas was controlled. This was checked by the inspection team.

INJ I was inspected during the inspection. INJ I was dedicated for dispensing and filling of Artesunate - sterile bulk powder (in cans) and the finished dosage form (in vials). INJ II was a multi-product filling workshop for different sizes of ampoules.

**INJ VI**

INJ VI was located in a separate building. Access was controlled. INJ VI was inspected. The production facilities were renovated and production was started at the end of 2016. The new autoclave was qualified. HVAC balancing and monitoring system was upgraded. Ground floor was used for storage of semi-finished products. Multi-product filling workshop was located on the second floor.

Labelling of Artesunate vials was done in INJ-I workshop, while labelling of Sodium bicarbonate and Sodium chloride ampoules was done in INJ II workshop.

**Co-packaging center for Artesunate vials with Sodium bicarbonate and Sodium chloride ampoules**

The building previously called INJ V had been reconstructed. The previous INJ V production workshop had been dismantled. The co-packaging centre had been created for Artesunate injection products (including

Artesunate powder for injection vials with solvent and diluent: Sodium bicarbonate and Sodium chloride ampoules). Reconstruction works were finished in September – October 2016. Co-packaging operations in the reconstructed building started in December 2016. Co-packaging centre was inspected during the inspection. The premises were spacious with a number of storage rooms. Co-packaging was done manually and on semi-automated packaging machines.

Quality control areas

Sufficient space was given to avoid mix ups and cross-contamination. Storage space was provided for samples, reference standards, solvents, reagents and records. QC laboratory was separated from the production. Penicillin's QC was located in the Penicillin's building.

Microbiological laboratory was separate from chemical laboratory. Laboratory was spacious. Separate rooms were provided for media preparation and sterilization. Incubation was carried out in several rooms. Incubators were connected to the wireless alarm system and temperature was recorded every 5 minutes. Separate rooms were provided for sterility test, endotoxin tests, microbial limit test and growth promotion test. Master cultures were stored in a separate room.

**13. Equipment**

Fixed pipework was labelled to indicate the contents and the direction of flow. Balances and other measuring equipment of an appropriate range and precision were available for production and control operations and were calibrated on a scheduled basis.

Closed RABS and open RABS were used for aseptic operations.

**14. Materials**

Materials were received, sampled and tested according to written procedures.

**15. Documentation**

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

The SOP "Environmental monitoring, production INJ I" was discussed. Settle plates and air sampling points were selected based on the RA. Risk assessment for INJ I was discussed. Risk assessment (RA) was performed using FMEA.

Settle plates (TSA) exposure time validation report was discussed. Settle plates with TSA were purchased readymade from medium supplier. During the validation settle plates in grade A were exposed for 5 hours.

The SOP "Clean room laundry, drying tiding and sterilization" was discussed. According to the SOP purified water was used for laundry.

The SOP "Sterile gloves test procedure" was discussed. Each batch of gloves received was tested according to the SOP and ISO 10282-2014. Sterile gloves CoA was also discussed.

The SOP "Hydrogen peroxide fumigation procedure for INJ I and INJ II" was discussed. The fumigation procedure was applicable for grade B, C and D rooms. According to the SOP fumigation should be done once per month.

The SOP "Cleaning and testing procedure for gloves used in ORABS" was discussed. Gloves were cleaned and disinfected daily after production. All gloves integrity tests were performed once per month, followed by area fumigation.

The SOP "Disinfectant preparation and usage" was discussed.

The SOP "Compressed air" was discussed. Compressed air came into contact with sterilised surfaces and the utility was placed under appropriate control.

The SOP "Sterile powder filling weight test procedure" was discussed.

The SOPs "Ampoules sampling and testing" and "Vials sampling and testing" were discussed. Sampling was carried out according to the AQL sampling level I.

**16. Good practices in production**

In general production operations followed defined procedures.

The production areas inspected (INJ I, INJ II and INJ VI) were generally designed and maintained to ensure flow of materials and personnel.

The aseptic powder filling line INJ I was dedicated for dispensing and filling of Artesunate - sterile bulk powder (in cans) and the finished dosage form (in vials).

Inspectors monitored set up of the vial filling line (excluding assembly of the line) and start-up of the filling process. Powder filling was done in grade A within open restricted access barrier system (ORABS). Operators were appropriately gowned for grade A and B clean rooms. Operators were moving slowly and the aseptic techniques observed were acceptable.

Batch manufacturing records (BMR) used in class B rooms were sterilized.

Inspectors monitored unloading of sterile Artesunate API powder/bulk from the lyophiliser. Unloading was done in ORABS. After unloading, the sterile powder was transferred to the powder collection tank using vacuum. From the collection tank the sterile powder was transferred (using vibration) to CRABS unit for filling into cans.

Sterilization in place (SIP) procedures were established.

## 17. Good practices in quality control

General

The QC function was independent from other departments. Adequate resources were available to ensure that all QC arrangements were carried out in a timely and orderly fashion. QC personnel had access to production areas for sampling and investigations as appropriate. All HPLCs and GCs were using Empower 3 software and were connected to the server system. IRs and UVs were standalone instruments.

The SOP "Electronic data management" was discussed. This SOP also explained the conditions applicable for manual integration (MI). MI was allowed only for relative substances, impurities and residual solvents. In case MI was deemed necessary, the analyst was to record this in the analytical work sheet, inform the supervisor and after written approval perform MI. The SOP specified daily electronic data review. Data review was performed by reviewer and recorded in data review log books specific to the equipment. Data review log book was spot checked.

The SOP "Empower 3 software management procedure" was discussed. There were 5 access levels specified for software access.

The SOP "Standard management procedure for materials and product release" was discussed.

Reference standards

Reference and working standards were available, stored in a refrigerator, usage was recorded. Working standards (WS) were qualified against pharmacopoeia reference standards.

Out of specification results (OOS) and our of trends (OOT)

The SOP "Investigation procedure for OOS and OOT" was applicable for all investigation of OOS/OOT results of raw materials and excipients, packaging materials, APIs, intermediates, validation samples, water for pharmaceutical uses, gases and environmental monitoring, finished products and stability studies. SOP and its flow chart were discussed. This procedure was also applicable for microbiological OOS tests and sterility failure. It did not cover IPC activities in production. The SOP stated that OOS/OOT should be trended annually.

Common OOS/OOT logbook/register was used for the chemical and microbiological labs (practicality of such arrangement was discussed). OOS/OOT registers for 2016 and 2017 were presented to the inspectors. The Company had amended their approach to OOS; the logbooks included considerably more cases than in the past. Re-run (same sample solution) and re-test (sample prepared anew) principles were established. Investigations into production were included in the SOP.

OOS/OOT were trended, trends for 2016 were presented to inspectors.

Back up of electronic data

The SOP "Computer system back-up and restoration" was discussed.

## PART 3

***CONCLUSION***

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection, Guilin Pharmaceutical Co. Ltd production workshops*:* INJ-I, INJ-II, INJ-VI, Co-packaging center for Artesunate for Injection, located at No.43, Qilidian Road, Guilin, Guangxi, China, 541004 was considered to be operating at an acceptable level of compliance with WHO good manufacturing practices for pharmaceutical products.

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

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

## PART 4

***List of GMP guidelines used for assessing compliance***

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

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

3. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2.
   ***Short name: WHO TRS No. 957, Annex 2***
   http://www.who.int/medicines/publications/44threport/en/

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

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

6. WHO guidelines on good manufacturing practices for heating, ventilation and air-conditioning systems for non-sterile pharmaceutical dosage forms. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 5
***Short name: WHO TRS No. 961, Annex 5***
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

7. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4
***Short name: WHO TRS No. 937, Annex 4***
http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf?ua=1

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

9. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2
***Short name: WHO TRS No. 957, Annex 2***
http://www.who.int/medicines/publications/44threport/en/

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

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

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

13. WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2
***Short name: WHO TRS No. 961, Annex 2***
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

14. WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2
***Short name: WHO TRS No. 981, Annex 2***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

15. WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3
***Short name: WHO TRS No. 981, Annex 3***
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