World Health Organization

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Prequalification Unit – Inspection Services
WHO PUBLIC INSPECTION REPORT
Contract testing laboratory

Part 1	**General information**
Contract testing laboratory	
Name of the laboratory	PT. Sanbe Farma Laboratory - Unit 3 - Sterile Preparations Plant
Address	Jl. Industri Cimareme No. 8 Block A, Bandung Barat – Bandung Indonesia. Post code (Zip code): 40553 North latitude: 6,865159 East longitude: 107,494871 D-U-N-S: 728716168
Corporate address of manufacturer/laboratory	Jl. Purnawarman No. 47 Bandung 40116 Indonesia Phone: 62 22 4207725 Fax: 62 22 4222928
Dates of inspection	27 - 28 January 2020
Type of inspection	Initial inspection for testing oral solid dosage forms. *Note: Laboratory site was inspected for testing sterile products*
Brief description of the quality control activities	The laboratory was involved in the testing of starting materials, in process and finished products as: • Tablets, coated tablets and effervescent tablets • Liquids • Semi solids • Sterile products
General information about the laboratory	Laboratory was located at PT Sanbe Farma Unit 3 (Sterile Preparations Plant). The following laboratories were identified: • Chemical/instrumental testing of PT Sanbe Farma Unit 3 products • Chemical/instrumental testing of PT Caprifarmindo Laboratories Products (contract testing, named as Sanbe Toll Laboratory) • Chemical/instrumental testing of PT Sanbe Farma Unit 1 products • Microbiological laboratory Note: PT Sanbe Farma Unit 2 - Beta lactam site had their own QC laboratory
History	This was the first WHO inspection of the QCL of the site which is used as contract laboratory for testing of the solid dosage form – coated tablets
Areas inspected	See Part 2 below
Restrictions	Products not related to PQ
Out of scope	Production activities at PT Sanbe site
WHO products numbers covered by the inspection	Testing of Levofloxacin tablet, film-coated 500 mg

Abbreviations	Meaning
ADE	Acceptable daily exposure
ADR	Adverse drug reaction
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APQR	Annual product quality review
AQL	Acceptance quality limit
BMR	Batch manufacturing record
BPR	Batch production record
CAPA	Corrective and preventive action
CC	Change control
CCEA	Complete, consistent, enduring, available
CFU	Colony-forming unit
CIP	Cleaning in place
CoA	Certificate of analysis
Cpk	Process capability
CPP	Critical process parameter
CQA	Critical quality attribute
DQ	Design qualification
EM	Environmental monitoring
FBD	Fluid bed drier
FMEA	Failure modes and effects analysis
FMECA	Failure mode, effects and criticality analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis
GC	Gas chromatograph
GMP	Good manufacturing practices
GPT	Growth promotion test
HACCP	Hazard analysis and critical control point
HAZOP	Hazard operability analysis
HDPE	High density polyethylene
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
LoD	Loss on drying
MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae
MR	Management review

NC	Non-conformity
NCA	National control authority
NCL	National control laboratory
NIR	Near infrared spectroscopy
NRA	National regulatory agency
OOS	Out of specification
OOT	Out of trend
OQ	Operational qualification
PD	Pressure differential
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
QP	Qualified person
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
RO	Reverse osmosis
RPN	Risk priority number
RSD	Relative standard deviation
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
USP	United States Pharmacopoeia
UV	Ultraviolet-visible spectrophotometer
VMP	Validation master plan
WS	Working standard

Part 2	Summary of the findings and comments

1. Quality system

Principle

Control operations were specified in written form and GMP requirements were essentially being met. Regular monitoring and reviews of the quality of pharmaceutical products were being conducted according to documented schedules and procedures.

Electronic data back-up and restoration of electronic data

Corporate procedure "Lab solution data back-up and restoration" was discussed. Data restoration exercise was recorded, report dated 20/09/2019 was presented.

SOP "Audit trail in HPLC which use LC solution" was discussed.

Disaster management

SOP "Computer backup and data recovery - Disaster management" was discussed.

Access control and security policies for different computer systems

The following SOPs were discussed:

- SOP "Operating procedure of Lab Solution client server" was discussed. Four access levels were specified
- "UV and FTIR security access level"
- "HPLC and GC security access level"
- "Good Chromatographic practice"
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Data integrity policy (DIP)

Document "Sanbe Farma Unit 3 (Sterile Preparation Plant) data integrity policy" was briefly discussed. DIP was applicable for all departments including QC/QA.

2. Facilities and equipment system

Laboratories were separated from production areas and were of suitable size. Microbiological laboratory was separated from chemical/physical laboratory. Equipment, instruments and other devices were designed, constructed, adapted, located, calibrated, qualified, verified and maintained as required by the operations to be carried out.

Chemical / Physical Laboratory premises and equipment

Laboratory premises were seen to be spacious and clean. Access was fingerprint controlled. Wet chemical laboratory was separated from instrumental laboratories. Laboratories were designed to suit the operations to be carried out in them. Sufficient space was given to avoid mix ups and cross- contamination. Suitable storage space was provided for samples, reference standards, solvents, reagents and records.

Microbiology Laboratory premises and equipment

The Microbiology Laboratory was located adjacent to the Chemistry Laboratory (entrance shared) with several different laboratories. Access to the Microbiology Laboratory was restricted to authorized personnel. Sterility testing was performed in a dedicated area.

Calibration

The following equipment calibration activities were discussed:

- Analytical balance
- Dissolution

3. Laboratory control system

Contact analysis agreement with contract laboratory PT. Sanbe Farma, located at Jalan Industri Cimareme Block A No. 8, Bandung, Indonesia" was discussed. Parties responsibilities were specified.

Lab Solution software validation

HPLC were operated by Lab Solution software version 6.82.SP1, installed 20/04/2018. The following documents were available and briefly checked:

- URS: Approved 18/05/2017
- DQ: Approved 12/02/2018
- IQ: Approved 12/03/2018 before DS by Shimadzu.
- Design specification (DS): Approved 05/05/2018 (Performed by Shimadzu)

OOS investigation

SOP "Investigation of out of specification", its flow chart and registers for 2017, 2018 and 2019 were discussed. SOP was applicable to starting materials, packaging materials, intermediates, bulk and finished products, sterility testing of finished products. SOP applies to both the chemical and microbiological testing.

Out of Trends (OOT) investigations

SOP "OOT" was briefly discussed.

Laboratory incidents

SOP "Laboratory incidents handling" and lab incidents logbook briefly discussed. Incidents were reported monthly.

Stability studies

The following documents were discussed:

- SOP "Stability testing program"
- Stability study protocol Levocin® 500 mg film-coated tablets
  - 40 ± 2 °C / 75 % ± 5 % RH
  - 30 ± 2 °C / 75 % ± 5 % RH
- Stability study report for Levocin® 500 mg film-coated tablets

Reference standards

SOP "Reference standard and working standard (WS)" was briefly discussed. WS were dispensed in amber color vials to be used within one month.

Microbiology laboratory
Organization and personnel
Discussed the Quality Control Organization Chart of the QC Laboratory for PT. Sanbe Farma Unit 3

Job description for the Non-Sterile Microbiological Supervisor was discussed.

Qualification of personnel
QC Manager Microbiology: Minimum of a bachelor's degree required.
Sterile Microbiological Manager: Minimum of a bachelor's degree required.
Microbiological Laboratory Analyst: Technical school for pharmaceutical assistant (No tertiary education)

Training
SOP "Training" was discussed.
Training was required to be conducted by the experts or competent person or by the supervisor of the employees.

Reviewed the Performance Qualification Protocol for autoclave and laminar air flow unit.

Part 3	**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, a decision on ***PT. Sanbe Farma Laboratory, (Unit 3)***, located at ***Jl. Industri Cimareme No. 8 Block A, Bandung Barat Indonesia*** was considered to be operating at an acceptable level of compliance with WHO GPPQCL Guidelines.

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

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

Part 4	List of WHO Guidelines referenced in the inspection report

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

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

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

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

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

6. WHO 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

7. 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

8. 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

9. 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

10. 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

11. WHO Guidelines for preparing a laboratory information file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report. Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 2011), Annex 13.
Short name: WHO TRS, Annex 13
http://www.who.int/medicines/areas/quality_safety/quality_assurance/GuidelinesPreparingLaboratoryInformationFileTRS961Annex13.pdf?ua=1TRS%20961:%20Annex%2013:%20WHO%20guidelines%20for%20preparing%20a%20laboratory%20information%20file