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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	Svizera Labs Private Limited Plot D 16/6, TTC Industrial Area MIDC, Turbhe, Navi, Mumbai – 400703, India D-U-N-S: Number of the site: - 72-533-7690 Latitude (19.0538) & Longitude (72.99777)
Corporate address of manufacturer	Svizera Labs Pvt. Ltd. Corporate Office: Plot 29 – 33, Ancillary Industrial Plots, Govandi, Mumbai 400043, India T: +91 22 25526500 F: +91 22 25526530
Inspected site	
Address of inspected manufacturing site if different from that given above	As above
Manufacturing license number	• Form 28, License No. KD – 315 for the drugs, being drugs specified in Schedule C & C (1) [excluding those specified in Schedule X] to the Indian Drugs and Cosmetic act, 1940 Rules,1945 • Form 25, License No. KD – 428 for categories of drugs being drugs other than those specified in Schedules C, C (1) and X to the Indian Drugs and Cosmetic Act, 1940 Rules,1945.
Inspection details	
Dates of inspection	25 – 29 June 2017
Type of inspection	Routine
Introduction	
Brief summary of the manufacturing activities	Production and control of finished dosage forms: • Tablets
General information about the company and	Svizera is part of Maneesh Pharmaceuticals Ltd. with the latter having the following manufacturing facilities: • Maneesh Pharmaceuticals Unit I, located at Govandi Mumbai, India (tablets,

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site	capsules, lotions. Creams, ointments, syrups, powders for suspension, injections, sterile powder for injections) • Maneesh Pharmaceuticals Unit II, located at Govandi Mumbai, India (Soft gelatin capsules, creams and ointments, gels) • Maneesh Exports (EOU) Unit III Betalactums/ Penicillins, located at Turbhe, Navi Mumbai, India (tablets, capsules, dry syrups. Dry powder injection single dose, water for injection) • Maneesh Pharmaceuticals Unit IV. Located Bhosari Pune, India (liquid orals) • Maneesh Pharmaceuticals Ltd. Unit VI. Located at Baddi, India (tablets, capsules, powders, effervescent tablets, dry syrups, injections) • Phaarmasia Ltd. Unit I, located at Hyderabad, India (cosmetics -Personal care & home care) • Phaarmasia Ltd. Unit II, located at Hyderabad, India (Hormones Oral Contraceptive pills)
History	The site was inspected by WHO: • November 2002 • March 2004 • November 2005 • March 2007 • September 2008 • September 2011 • June 2015 • June 2017 The site was inspected by MHRA • March 2011 • August 2012 The site was inspected by the following regulatory authorities after the last MHRA inspection in 2012: • December 2012 Pharmacy and Poisons Board Ministry of Medical Services (Republic of Kenya) • May 2013 FDA Maharashtra, India • August 2015 CDSCO, India • July 2016 FDA USA
Brief report of inspection activities undertaken	
Scope and limitations	
Areas inspected	See Part 2 below
Dosage form covered by the	Tablets for TB treatment

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inspection

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

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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

This inspection was WHO and MHRA joint inspection. Inspection focussed on issues related to the NOC, 23 July 2015 and data integrity.

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1. Pharmaceutical quality system (PQS)

Principle

Production and control operations in general were specified in written form. Managerial responsibilities were specified in job-descriptions.

Quality Risk Management (QRM)

QRM procedure was available.

Management review (MR)

MR was in place.

Deviations and corrective and preventive actions (CAPA)

Deviations and CAPA procedures were available.

Change control

CC procedure was available.

Product Quality Review (PQR)

PQR according to SOP Annual product quality review SOP was mostly similar to the items requested in chapter Pharmaceutical Quality System of the WHO good manufacturing practices for pharmaceutical products: main principles. A number of PQRs were reviewed for both markets WHO and EU. Deficiencies were noted.

2. Good manufacturing practices for pharmaceutical products

Generally manufacturing processes were defined and reviewed. Significant deviations were recorded and investigated. Systems were in place for handling complaints and recalling any batch of product from sale or supply. Deficiencies were noted.

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 was performed.

4. Qualification and validation

The company had identified what qualification and validation work was required and this was described in its Validation Master Plan. A number of process validation and cleaning validation studies were reviewed. Deficiencies were noted.

Production equipment cleaning

The check on the cleanliness of equipment and the absence of the previous API, with solvents used to collect the swabs and rinse the equipment. The solvents were specific and unique to the previous product manufactured. Deficiencies were noted.

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Air handling system

The annual verification of the 23 HVAC according to the SOP, Monitoring of HVAC system was studied. The last verification was done in November 2016 and subcontracted to an ISO 14644 certified company. The reports showed that the integrity of the HEPA filters were tested using PAO solutions in their operational conditions and that all the 23 filters passed the test. There was no microbiological contamination detected. According to the test results, all the rooms supplied with air from each of the 23 HVAC were tested and found ISO 8 at rest with recover time to ISO 8 within minimum 6 and maximum 8 minutes after particulate contamination. Deficiencies were noted.

5. Complaints

Procedure for complaints was available.

6. Product recalls

Procedure for recalls was available.

7. Contract production, analysis and other activities

Not inspected.

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

Procedure for self-inspection was available.

Vendor approval procedure

The Vendor Approval SOP was reviewed. The SOP did list the responsibilities of the Head of purchase, the Head of QA and Head of QC and the process to be followed to qualify a vendor starting from the analysis of pre-purchase simples up to the vendor suitability report. The API's stored in the warehouse on the day of the inspection were all purchased from qualified vendors. Deficiencies were noted.

9. Personnel

Generally, there were an adequate number of personnel qualified to perform and supervise the current level of manufacturing and its quality control.

10. Training

Training records of personnel met during the inspection, confirmed that the personnel were given training appropriate to the duties assigned to them.

Records were maintained which included basic principles of GMP and applicable SOP's. The trainers were habilitated and the trainer habilitation certificate was included in the training report. Generally, SOP's were not translated in the local language. Emergency messages in the premises were displayer in English and the local language. Deficiencies were noted.

11. Personal hygiene

Direct contact between the operator's hands and starting materials, primary packaging materials and intermediate or bulk products were avoided. Smoking, eating, drinking, chewing, and keeping plants, food, drink, smoking material and personal medicines were prohibited in production, laboratory and storage areas.

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12. Premises
The Svizera premises were old and require renovation in certain areas.

Manufacturing area
Production area and functioning equipment was inspected. This included the only functioning tablet compression machine in compression room XX. Air handling units were installed adjacent to the core processing areas and were accessible from production areas with some from the ceiling where an unsealed panel were opened to give access (with a ladder) to an approximatively 2.5 m high space were all maintenance was done. Other units installed in the walls of the processing areas required unscrew of panels which was found unacceptable. This matter had been raised during the previous WHO inspections in 2011 and 2015 and was not adequately addressed.

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

14. Materials
Materials were received, sampled and tested according to the written procedures. Deficiencies were noted.

15. Documentation
Documents were available which included SOPs, protocols and records. SOPs were generally followed with no major violations noted during the inspection.

Batch manufacturing records review
A number of batch records were reviewed with corresponding “Incident reviews”, deviations, change control, market complains and other issued when relevant. Deficiencies were noted.

16. Good practices in production
Generally, production operations followed defined documented procedures. Deviations from procedures were recorded and investigated.

17. Good practices in quality control
The QC function was independent from other departments. Adequate resources were available to ensure that all the QC arrangements were carried out. QC personnel had access to production areas for sampling and investigations.

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 Report, Svizera Labs Private Limited, located at Plot D 16/6, TTC Industrial Area MIDC, Turbhe, Navi, Mumbai – 400703, India was considered to be operating at an acceptable level of compliance with WHO good manufacturing practices for pharmaceutical products.

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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.
   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 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

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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 3
   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

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

15. WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3
Short name: WHO TRS No. 981, Annex 3
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

16. WHO guidelines for drafting a site master file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 14
Short name: WHO TRS No. 961, Annex 14
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

17. WHO Guidelines on good manufacturing practices: validation, Appendix 7: non-sterile process validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 3
Short name: WHO TRS No. 992, Annex 3
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

18. WHO General guidance on hold-time studies WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4
Short name: WHO TRS No. 992, Annex 4
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

19. WHO Technical supplements to Model Guidance for storage and transport of time – and temperature – sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 5
Short name: WHO TRS No. 992, Annex 5
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

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20. WHO Recommendations for quality requirements when plant – derived artemisin is used as a starting material in the prosecution 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
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

21. WHO good manufacturing practices for biological products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 3
Short name: WHO TRS No. 996, Annex 3
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex03.pdf

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

23. 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

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