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Prequalification Unit Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Desk Assessment of Finished Pharmaceutical Product (FPP) Manufacturer

Part 1	**General information**		
Company information			
Name of Manufacturer	MSN Laboratories Private Limited ("MSN")		
Corporate address of manufacturer	MSN House, Plot No.: C-24, Industrial Estate, Sanath Nagar, Hyderabad - 500 018, Telangana, India. Tel: +91-40-30438660 *Fax: +91 -40-30438798*		
Inspected site			
Name & address of manufacturing site	Survey # 1277, 1319-1324 Nandigama (Village & Mandal) Rangareddy District Telangana, 509228 India		
Production Block/Unit	Formulations Division, **Unit-II**, General Oral Solids Manufacturing Facility **(Block-D)**		
Desk assessment details			
Date of review	1 May 2020		
Products covered by this desk assessment	HA723	Darunavir Tablet, Film-coated 400mg	Under assessment
	HA724	Darunavir Tablet, Film-coated 600mg	Under assessment
	HA725	Darunavir Tablet, Film-coated 800mg	Under assessment
	IN018	Oseltamivir (phosphate) Capsules, hard 30mg	Under assessment
	IN019	Oseltamivir (phosphate) Capsules, hard 45mg	Under assessment
	IN020	Oseltamivir (phosphate) Capsules, hard 75mg	Under assessment
	TB338	Levofloxacin Tablet, Film-coated 250mg	Prequalified
	TB339	Levofloxacin Tablet, Film-coated 500mg	Prequalified
	TB340	Levofloxacin Tablet, Film-coated 750mg	Prequalified
	TB341	Moxifloxacin (hydrochloride) Tablet, Film-coated 400mg	Prequalified

Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last)**	
U.S. Food & Drug Administration	Dates of inspection:	4-15 November 2019
	Type of inspection:	Routine surveillance inspection
	Block/Unit:	Block D & Block - C,
	Type of products/Dosage forms covered:	General Oral Solids Manufacturing Facility & Oncology injectables

National Institute of Pharmacy and Nutrition, Hungary	Dates of inspection:	16-19 December 2019
	Type of inspection:	GMP inspection in connection with marketing authorization(s) listing manufacturers located outside of the European Economic Area. The inspection covered the manufacturing of oral solid dosage forms, tablets and capsule for human use, including oncology products.
	Block/Unit:	The non-sterile products were manufactured in two blocks, Block D general oral solid dosages (Block C dedicated to oncology products was out of scope of this inspection).
	Type of products/Dosage forms covered:	Oral solid dosage forms
U.S. Food & Drug Administration	Dates of inspection:	4-8 March 2019
	Type of inspection:	Pre-approval inspection for Empagliflozin and Metformin Hydrochloride ER Tablets
	Block/Unit:	Block D
	Type of products/Dosage forms covered:	Oral dosage form
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	20-23 March 2017 Compliant	
Brief description of manufacturing activities	Block D (Total built-up area:15550 m^2)	Ground floor - Warehouse, Change rooms, administration. ~ 4300 m^2 Mezzanine floor - QA, Conference hall, training hall, visitors dining, technical area. ~ 2645 m^2 First floor - QC and production area. ~ 4300 m^2 Second floor - Purified water system, stability chambers room, control samples room, AHUs technical area, offices. ~ 4300 m^2
	The site is authorized to manufacture tablets and capsules of General therapeutic category in Block-D, which is dedicated for Oral Solid Dosage (OSD) products.	

General information about the company and manufacturing site	MSN Laboratories Private Limited, Formulations Division, Unit-II, Nandigama is a unit of MSN Laboratories Private Limited and it belongs to MSN Group of companies established in the year 2003. MSN Group comprises several API manufacturing plants, two finished dosage facilities and a separate dedicated Research & Development center. Currently, the site contains five major independent buildings. Two of them are manufacturing blocks (Block C and Block D). Details of the five blocks are as follows; a) Block A: Security building b) Block B: Boiler House c) Block C: Manufactures Oncology Drug Products **d) Block D: Manufactures General Drug Products** e) Block E: Utility block f) Block G: Manufactures General Injectable
Focus of the last WHO inspection	Levofloxacin Tablet, Film-coated 250mg (TB338) Levofloxacin Tablet, Film-coated 500mg (TB339) Levofloxacin Tablet, Film-coated 750mg (TB340) Moxifloxacin Tablet, Film-coated 400mg (TB341)
Areas inspected	Pharmaceutical quality system Personnel Qualification and validation Quality control Production
Out of scope and restrictions (last WHO inspection)	Block C (oncology) and other areas out of scope of WHO PQ Area currently under expansion in Block D
WHO products covered by the last WHO inspection	1. Levofloxacin Tablet, Film-coated 250mg (TB338) 2. Levofloxacin Tablet, Film-coated 500mg (TB339) 3. Levofloxacin Tablet, Film-coated 750mg (TB340) 4. Moxifloxacin Tablet, Film-coated 400mg (TB341)
Additional products covered by this desk assessment:	1. HA723 (Darunavir Tablet, Film-coated 400mg) 2. HA724 (Darunavir Tablet, Film-coated 600mg) 3. HA725 (Darunavir Tablet, Film-coated 800mg) 4. IN018 (Oseltamivir (phosphate) Capsules, hard 30mg) 5. IN019 (Oseltamivir Capsules, hard 45mg) 6. IN020 (Oseltamivir (phosphate) Capsules, hard 75mg)

Abbreviations	Meaning
AHU	Air handling unit
API	Active pharmaceutical ingredient
BMR	Batch manufacturing record
BPR	Batch production record
CAPA	Corrective and preventive action
CC	Change control
GMP	Good manufacturing practices
NC	Non conformity
NRA	National regulatory agency
PQR	Product quality review
PQS	Pharmaceutical quality system
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
SOP	Standard operating procedure

Part 4	Summary of the assessment of supporting documentation

a) Manufacturing authorization and GMP certificate granted by the local authority:

Manufacturing authorization and GMP certificate granted by local national authority i.e. Drugs control administration (DCA), Telangana, India.

b) Site master file (SMF):

Site master file (SMF) of manufacturing facility has been provided. Site Master file is common for block – C and Block – D. (Block C is dedicated for oncology solid and sterile products). Water treatment and air-handling system including pipeline and instrumentation drawings with legible colour printouts have been provided. In general, the SMF appeared to be satisfactory and provided a high-level overview of the manufacturing activities carried out at Unit-II of MSN.

c) List of regulatory inspections performed in the last 3 years and their outcome:

Name of the Authority	Date of Inspection	Outcome Status
US FDA	25th Jan to 03rd Feb 2017	EIR received
Czech Republic	03rd to 06th April 2017	Certificate received
US FDA	17th to 21st July 2017	EIR received
US FDA	20th to 28th Feb 2018	EIR received
US FDA	04th to 08th March 2019	EIR received
US FDA	04th to 15th Nov 2019	EIR received
OGYEI, Hungary	16th to 19th Dec 2019	EU GMP received

d) List of all the products and dosage forms manufactured on-site:

The list of all products and dosage forms manufactured on-site are provided**.** The manufacturer confirmed that they intend to submit PQ applications from only D block (general non-sterile).

e) Most recent product quality review(s) (PQR)(s) of the concerned WHO product(s):

The applicant confirmed that no batches have been manufactured for the products Oseltamivir phosphate 30 mg, 45 mg and 75 mg hard capsules, Levofloxacin 250 mg, 500 mg and 750 mg film coated tablets and Darunavir 400 mg, 600 mg and 800 mg film coated tablets till date. Hence, APQR for these products are not available.

The APQR for Moxifloxacin 400mg tablets for 2018 was provided. A total of 2 batches (DT1809019 and DT1811024) were produced which were packed in 4 batches (DTI809019A, DTI811024A, DTl811024B and DTl811024C).

f) Batch manufacturing and packaging record(s), including the analytical part, for the most recently released batch of relevant product(s):

Out of all the submitted products to WHO, only Moxifloxacin 400 mg filmcoated tablets has been manufactured and commercialized. Most recently released batch manufacturing (DT191009 and DT1910020) and packing (DT1910019A, DT1910019B, DT1910019C, DT1910019D and DT1910020A) records along with analytical test results for Moxifloxacin 400mg film-coated tablets have been provided

g) Master batch manufacturing and packaging record(s) of the product(s) of interest:

The master batch manufacturing (BMRs) and packing records (BPRs) of WHO products (Darunavir, Levofloxacin, Moxifloxacin and Oseltamivir) of interest has been provided

h) Recalls in the past three years related to products with quality defects:

The applicant confirmed that there are no product recalls in the past three years related to any product manufactured in site with quality defects.

i) Confirmation by the senior quality assurance representative that a full self-inspection or external audit dedicated to the product(s) has been performed and all matters dealt with:

The applicant confirmed that a full self-inspection has been performed covering all areas / systems of all functional departments as per internal defined procedures and for all the observations were handled through CAPA system and closed appropriately. In addition, the external audits by health authorities were conducted to our site covering all the lines of our site related to D-Block (General Oral Solids) and all the observations related were closed and obtained the close-out reports.

j) Copy of any warning letter, or equivalent regulatory action, issued by any authority to which the site provides or has applied to provide the product:

The applicant has confirmed that there is no warning letter or equivalent regulatory action, issued by any authority to site regarding any product.

k) Out-of-stock situations:

The applicant has confirmed that we have not faced any recent or foreseen out of stock situations.

l) Additional documents submitted:

The applicant has confirmed that there is no planning of any GMP inspections for forthcoming 6 months.

Part 5	**Conclusion – Desk assessment outcome**

Based on the previous WHO inspections and on the GMP evidence received and reviewed, it is considered that a desk assessment is acceptable in lieu of a WHO onsite inspection. The site ***MSN Laboratories Private Limited, Formulations Division, Survey # 1277, 1319-1324, Block D, Nandigama (Village & Mandal) Rangareddy District Telangana, 509228 India*** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines.

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

Part 6	List of guidelines referenced in this inspection report

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eighth 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 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 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***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

20. 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

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

22. 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

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

24. 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

25. Points to consider for manufacturers and inspectors: environmental aspects of manufacturing for the prevention of antimicrobial resistance. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 6.
Short name: WHO TRS No. 1025, Annex 6
https://www.who.int/publications-detail/978-92-4-000182-4

26. WHO guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report. Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 9. ***Short name: WHO TRS 1010, Annex 9***
https://www.who.int/medicines/areas/quality_safety/quality_assurance/TRS1010annex9.pdf?ua=1