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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	Mylan Laboratories Limited	
Corporate address of manufacturer	Mylan 1000 Mylan Boulevard Canonsburg PA 15317 USA	
Inspected site		
Name & address of manufacturing site	Mylan Laboratories Limited (Specialty Formulation Facility) No. 19A, Plot No.284-B/1, Bommasandra-Jigani Link Road, Industrial Area, Anekal Taluk, Bangalore, 560105, India	
Production Block/Unit	Suite 4 (Kanamycin)	
Desk assessment details		
Date of review	20-22 October 2020; 16-17 November 2020; 27-29 January 2021	
Products covered by this desk assessment	TB343 Kanamycin (sulfate) Solution for Injection 500 mg/2 ml TB344 Kanamycin (sulfate) Solution for Injection 1000 mg/3 ml	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last)**	
USFDA, USA	Dates of inspection:	20 – 28 February 2020
	Type of inspection:	Pre-approval and post approval inspection
	Block/Unit:	Suites 1-3
	Type of products/Dosage forms covered:	Sterile injectables
USFDA, USA	Dates of inspection:	06 -13 May 2019
	Type of inspection:	Surveillance GMP inspection
	Block/Unit:	Suites 1-5
	Type of products/Dosage forms covered:	Aseptically prepared small volume parenterals, lyophilized injectables
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	The initial WHO inspection was conducted during 10 - 19 September 2018. The site was deemed GMP compliant	

Brief description of manufacturing activities	The site is authorized to manufacture, package, label, test and store of: • Sterile liquid parenterals in vials (aseptically filled) • Sterile liquid parenterals in vials (terminally sterilized) • Sterile lyophilized parenterals in vials • Sterile liquid parenterals in mini bags (terminally sterilized)
General information about the company and manufacturing site	The Specialty Formulation Facility (SFF) originally belonged to Strides Arcolab Limited and later to Agila Specialties Private Limited. It became operational in May 2009 and the first sterile products reached the market in 2011. It was acquired by Mylan in December 2013. Mylan has five injectable manufacturing sites located in and around Bangalore, India including SFF site.
Focus of the last WHO inspection	The inspection focused on Kanamycin inj. Production in Suite 4
Areas inspected	The inspection covered all six systems namely, Pharmaceutical quality system, Documentation system, Production system, Facilities and equipment system, Laboratory control system, Packaging and labelling system
Out of scope and restrictions (last WHO inspection)	N/A
WHO products covered by the last WHO inspection	TB343 Kanamycin (sulfate) Solution for Injection 500 mg/2 ml TB344 Kanamycin (sulfate) Solution for Injection 1000 mg/3 ml
Additional products covered by this desk assessment:	N/A
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:
The facility is authorized to manufacture sterile liquid parenterals, freeze dried/ lyophilized injectables and terminally sterilized liquid parenterals in vials and infusion bags.

b) Site master file (SMF):
The company provided a copy of the latest SMF revision valid until March 2022. In addition, the company provided as attachments to the SMF, the following documents:

1. Detailed layouts of the facilities
2. Schematic diagrams of AHU zoning
3. Schematic diagram of area classification
4. Schematic diagram of differential pressure
5. List of critical AHUs
6. Process flow for sterile liquids
7. Schematic diagrams for personnel and material movement
8. Diagram of PW system
9. Diagram of WFI system

Review of the above-mentioned diagrams did not give rise to any major concerns.

c) List of regulatory inspections performed in the last 5 years and their outcome:

No	Regulatory Authority	Inspection Date	Compliance
1	CDSCO, India	03-05.11.2015	Compliant
2	ZAZIBONA, SADC	03-05.12.2015	Compliant
3	CDSCO, India	24.03.2016	Compliant
4	USFDA, USA	04-13.04.2016	Compliant
5	CDSCO, India	08.09.2016	Compliant
6	TGA, Australia	21-26.11.2016	Compliant
7	USFDA, USA	10-18.04.2017	Compliant
8	Tanzania FDA	17-18.07.2017	Compliant
9	Libyan Ministry of Health	09-12.09.2017	Compliant
10	CDSCO, India	27-28.11.2017	Compliant
11	USFDA, USA	22.02-02.03.2018	Compliant
12	WHO	10-19.09.2018	Compliant
13	CDSCO, India	18-19.03.2019	Compliant
14	USFDA, USA	06-13.05.2019	Compliant
15	CDSCO, India	08.07.2019	Compliant
16	USFDA, USA	20-28.02.2020	Compliant

No	Regulatory Authority	Inspection Date	Compliance
17	CDSCO, India	19-20.06.2020	Compliant

d) List of all the products and dosage forms manufactured on-site:
The company is authorized to manufacture 617 terminally sterilized and aseptically prepared products. In addition, the company provided a list of 139 commercialized products. Most of these products are marketed in USA, Australia, Canada and India.

e) Most recent product quality review(s) (PQR)(s) of the concerned WHO product(s):
No Kanamycin batch has been manufactured since the product was prequalified. However, changes to master BPR took place in 2019.

f) Batch manufacturing and packaging record(s), including the analytical part, for the most recently released batch of relevant product(s):
No Kanamycin batch has been manufactured since the product was prequalified

g) Master batch manufacturing and packaging record(s) of the product(s) of interest:
Master batch and packaging records were provided both for Kanamycin (sulfate) Solution for Injection 500 mg/2 ml and 1000mg/3ml. The latest BMR versions became effective in March 2020. Similarly, BPRs were revised in April 2019.

h) Recalls in the past three years related to products with quality defects:
In the last three years one voluntary recall and one withdrawal took place. The recall was carried out in 2020. Additionally, one voluntary withdrawal was initiated in 2020 due to OOT results in stability studies

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 company confirmed that a self-inspection program is in place and it covers all six systems for all products manufactured on site including prequalified products. Self-inspections are performed according to an approved plan and cited observations are appropriately addressed by CAPAs. The confirmation is signed by the site's Head of Quality Assurance

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 company provided a confirmation that no regulatory actions have been taken against the site in the last three years

k) Out-of-stock situations:
No out of stock situations have occurred in the last three years and none is foreseen in the coming 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 ***Mylan Laboratories Limited (Specialty Formulation Facility)*** located at ***No. 19A, Plot No.284-B/1, Bommasandra-Jigani Link Road, Industrial Area, Anekal Taluk, Bangalore, 560105, India*** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines.

This compliance status shall be valid until January 2022 or when another inspection is conducted by WHO or by a stringent regulatory authority. It remains the prerogative of WHO to carry out an inspection any time prior to that.

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 3.
Short name: WHO TRS No. 957, Annex 3
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