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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Desk Assessment of Active Pharmaceutical Ingredient (API) Manufacturer

Part 1	**General information**	
Company information		
Name of Manufacturer	Symed Labs Ltd	
Corporate address of manufacturer	Symed Labs Ltd., 8-2-293/174/3, Beside BN Reddy Colony, Road No. 14, Banjara Hills, Hyderabad – 500 034 Telangana, INDIA	
Inspected site		
Name & address of manufacturing site	Symed Labs Ltd, Unit 1, Survey No 353, Domadugu, Gummadidala, Sanga Reddy, Telangana, 502 313, India17° 39’ 38.26”N, 78° 22’ 11.19” E DUNS: 65-053-0301	
Synthetic Unit/Block/ Workshop	Unit 1, Block A and Clean Room Building	
Desk assessment details		
Date of review	26 November 2018	
APIs covered by this desk assessment	Linezolid (Form II), Linezolid (Form III)	
List of documents submitted	-Response letter from Symed Labs Ltd. -Drugs Control Administration, Government of Telangana License -Site master file dated 16/04/2018 -Water and HVAC schematic diagrams -List of APIs manufactured on site -Documentation from US FDA inspection, including EIR. -APQRs for Linezolid -Declaration on self-inspection of facility, dated 29/08/2018 -Executed batch records for linezolid -Certificate of analysis	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last)**	
US FDA	Dates of inspection:	04/30/2018- 05/04/2018
	Type of inspection:	Routine re-inspection (previous inspection was on 06/2015)
	Block/Unit/Workshop:	Building Block A and Clean Room Building (this is where the APIs are isolated in reactors, centrifuges followed by drying,

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		milling and blending operations)
	Type of APIs covered:	Same APIs as those submitted to WHO Prequalification (Linezolid Form II and Linezolid Form III) and another API.
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	The last WHO inspection was performed 19-21 October 2015 and resulted in a declaration of GMP compliance.	
Brief description of manufacturing activities	Production and quality control of non-sterile intermediates and finished non-sterile APIs by chemical synthesis. No toxic or hazardous substances were manufactured on site.	
General information about the company and manufacturing site	Symed Labs Limited was established in 1998 and is involved in the manufacture and marketing of intermediates and active pharmaceutical ingredients (APIs). Symed Labs Limited has six (6) Units, located at: • Unit I - Survey No.353, Domadugu (Village), Jinnaram (Mandal), Medak (Dist) – 502 313. Telangana, India – inspected unit; • Unit II - Plot-25/B, Phase –III, I.D.A - Jeedimetla, Hyderabad-500055, Telangana, INDIA; • Unit III - Plot. No: 19, 20 & 21, Phase-I, I.D.A, Jeedimetla, Hyderabad-500055, Telangana, INDIA; • Unit IV - Survey.No 163 & 163/A,164/A, Pittampally (Village), Chityal (Mandal), Nalgonda (District)-508114, Telangana, INDIA; • Unit V Symed research centre - PlotNo-89/A, Phase- I, I.D.A, Jeedimetla, Hyderabad-500055, Telangana, INDIA; • Unit VI - Survey No. 744, 745, 750, 751, 752 & 753, Valigonda Road, Mandollagudem (Village), Chowtuppal (Mandal), Yadadri (District) - 508252, Telangana, INDIA At the time of the inspection, the number of persons working at Symed Labs was about 126 (including 20 contract workers), of which 42 were involved in production, 18 in quality assurance (QA) and 24 in quality control (QC).	
Focus of the last WHO inspection	Production and quality control of non-sterile intermediates and finished non-sterile APIs.	
Areas inspected	Production Block-A /Clean Room-II (The site had two production blocks: Block A and Block B There was a separate Clean Room building, with five clean rooms. It was	

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	commissioned in June 2013.)
Out of scope and restrictions (last WHO inspection)	Block B and other clean rooms were not covered
WHO APIs covered by the last WHO inspection	Linezolid (Form II)
Additional products covered by this desk assessment:	Linezolid (Form III)
Abbreviations	**Meaning**
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 Drugs Control Administration, Government of Telangana Licence was provided and is considered acceptable.

b) Site master file (SMF):
The site master file dated 16/04/2018 was reviewed and is considered acceptable.

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c) List of all the APIs or other products (intermediates, dosage forms) manufactured on-site:
No B-lactam antibiotics (penicillin and cephalosporin), steroids, hormones or cytotoxic compounds are produced or handled at this facility.

d) Current inspection report and GMP certificate issued by the USFDA:
Reviewed and considered acceptable.

e) Most recent product quality review(s) (PQR)(s) of the concerned WHO API(s):
Reviewed and considered acceptable.

f) Batch manufacturing and packaging record(s), including the analytical part, for the most recently released batch of relevant API(s):
Reviewed and considered acceptable.

g) Master batch manufacturing and packaging record(s) of the API(s) of interest:
Reviewed and considered acceptable.

h) Recalls in the past three years related to APIs with quality defects:
The company declared that there were no recalls in the past 3 years.

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

j) copy of any warning letter, or equivalent regulatory action, issued by any authority for their market, to which the site provides or has applied to provide the API(s):
Information provided was reviewed and considered acceptable.

k) Out-of-stock situations:
Information provided was considered acceptable.

l) Additional documents submitted:
Documentation on the comparability of the Linezolid API submitted to WHO PQ to the product that was inspected by the USFDA was reviewed and found acceptable.

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 ***Symed Labs Ltd, Unit 1, Survey No 353, Domadugu, Gummadidala, Sanga Reddy, Telangana, 502 313, India*** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines for APIs.

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**

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1. 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 GMP for APIs*** or ***TRS No. 957, Annex 2***
http://apps.who.int/medicinedocs/documents/s20119en/s20119en.pdf

2. 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 GMP Guidelines*** or ***WHO TRS No. 986, Annex 2***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

3. 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

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. 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/

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 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. 961, 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 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

11. 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

12. 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

13. 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

14. 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

15. 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/

16. 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/

17. 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

18. 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

19. 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

20. 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

21. 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.

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Short name: WHO TRS No. 996, Annex 5
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf

22. 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

23. 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

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