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

Part 1	**General information**
Company information	
Name of Manufacturer	R-Pharm Germany GmbH
Corporate address of manufacturer	R-Pharm Germany GmbH Heinrich-Mack-Str. 35 89257 Illertissen Germany +49730312582 +491727464613
Name & address of manufacturing site	R-Pharm Germany GmbH Heinrich-Mack-Straße 35, 89257 Illertissen, Germany GPS: 48° 13`59.8" N 10°5`19.1" E DUNS: 342784660
Production Block/Unit	Building A8
Desk assessment details	
Date of review	01 – 03 June 2020
Products covered by this desk assessment	Delamanid Tablet, Film-coated 50mg
List of documents submitted	1. SMF and its Appendixes 2. Government of Upper Bavaria GMP-Inspection report 3. CAPAs to Government of Upper Bavaria GMP-Inspection report 4. Government of Upper Bavaria GMP certificate 5. Table – packaging information Delamanid Tablet, Film-coated 50mg 6. Declaration: foreseen updates 7. Declaration: foreseen out-of-stock situations 8. List of regulatory authorities' inspections in last 5 years 9. List of products packed at site 10. List of upcoming inspections 11. Master BPR 12. PQRs Delamanid Tablet, Film-coated 50mg • Delamanid Tablet, Film-coated 50mg • Delamanid Tablet, Film-coated 50mg commercial forms • Delamanid Tablet, Film-coated 50mg yield data • Delamanid Tablet, Film-coated 50mg stability data 13. Manufacturing license 14. Declaration: recalls 15. Declaration: self-inspection 16. Declaration: warning letter 17. FDA EIR 18. Delamanid Tablet, Film-coated 50mg Batch No XX BPR

Part 2	**Summary of SRA/NRA inspection evidence considered**	
Government of Upper Bavaria, Germany	Dates of inspection:	26 – 27 February 2019
	Type of inspection:	GMP routine inspection
	Block/Unit:	Building D4 Building A1 (solid dosage form facility) Building A02 Quality control
	Type of products/Dosage forms covered:	Capsules Tablets
US Food and Drug Administration, USA	Dates of inspection:	29 July – 1 August 2019
	Type of inspection:	Surveillance inspection
	Block/Unit:	Building D4 Building A4 Building A8 (used for *Delamanid Tablet packaging)*
	Type of products/Dosage forms covered:	Tablets
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	The site has not been inspected by the WHO	
Abbreviations	**Meaning**	
BMR	Batch manufacturing record	
BPR	Batch production record	
CAPA	Corrective and preventive action	
GMP	Good manufacturing practices	
PQR	Product quality review	
APQ	Annual product review	
SMF	Site master file	
SOP	Standard operation procedure	
STP	Standards test procedure	
EIR	Establishment inspection report	
QP	Qualified person	

Part 4	**Summary of the assessment of supporting documentation**

a) Manufacturing authorization and GMP certificate granted by the local authority:
Manufacturing/Import License: DE_BY_04_MIA_2019_0128/ROB-53Ph-2677.Ph_2-258
GMP certificate: ROB-53Ph-2677.Ph_2-258-66

b) Site master file (SMF):
SMF submitted and reviewed. SMF written according to the WHO TRS No. 961, Annex 14

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

Name of regulatory authority	Dates of inspection	Outcome
US-FDA	06th-10th Feb 2017	Complies
Turkish Ministry of Health	06th-08th Jun 2017	Complies
Ministry of Trade and Industry of the Russian Federation	13th-15th Feb 2018	Complies
Pharmacy Poisons Board Republic of Kenya	21st Jun 2018	Complies
ANVISA Brazil	12th-16th Nov 2018	Complies
EMA, local Inspectorate Authorities of Upper Bavaria	26th-27th Feb 2019	Complies
US-FDA	29th Jul - 2nd Aug 2019	Complies
Ministry of Trade and Industry of he Russian Federation	29th - 31st Oct 2019	Complies
Ministry of Health of the Republic of Belarus	04th-05th Mar 2020	Complies

d) List of all the products and dosage forms manufactured (primary and secondary packaging) on-site:
Tablets: uncoated and coated
Capsules: hard gelatine
Therapeutically groups: selective calcium channel blocker with mainly vascular effects; anti-inflammatory and antirheumatic; relapsing forms of multiple sclerosis; antihypertensive antiadrenergic agent; analgesics; urologicals; drug used in nicotine dependence; antimycotics; pyknoleptic; tuberculosis; antidiarrheals; anti neoplastic; anticholinergic; immunosuppressor; antimetabolite

e) Most recent product quality review (PQR) of the concerned WHO product:
Submitted and reviewed PQRs for:

- Delamanid Tablet, Film-coated 50mg
- Delamanid Tablet, Film-coated 50mg commercial forms
- Delamanid Tablet, Film-coated 50mg yield data
- Delamanid Tablet, Film-coated 50mg stability data

f) Batch manufacturing and packaging record, including the analytical part, for the most recently released batch of relevant product:
Delamanid Tablet, Film-coated 50mg, batch No XX primary and secondary packaging and analytical part submitted and reviewed.

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

h) Recalls in the past three years related to products with quality defects:
Declaration submitted: no recalls

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:
Declaration submitted: self-inspection performed annually, all matters dealt with

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:
Declaration submitted: no warning letters issued

k) Out-of-stock situations:
Declaration submitted: no out-of-stock situations

Part 5	**Conclusion – Desk assessment outcome**

Based 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 ***R-Pharm Germany GmbH*****,** located at ***Heinrich-Mack-Straße 35, 89257 Illertissen,*** **Germany** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines for purposes of primary and secondary packaging.

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 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