World Health Organization

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Prequalification Unit Inspection services

WHO PUBLIC INSPECTION REPORT

Desk Assessment of Finished Product Manufacturer
(Secondary Packaging)

Part 1	**General information**
Company information	
Name of Manufacturer	Arvato Distribution GmbH
Inspected site	
Name & address of manufacturing site	Arvato Distribution GmbH Gottlieb-Daimler-Strase 1 33428 Harsewinkel, Germany GPS coordinates: 51° 58‘4,5“N 8° 15‘19,1“E
Packaging rooms	HJ1 S026 / HJ1 A012 / HJ1 A020
Manufacturing license number	DE_NW_02_MIA_2020_0001, issued 18/02/20
Desk assessment details	
Start and end dates of review	27 May 2020 and 4 August 2020
Products covered by this desk assessment	Delamanid Tablet, Film-coated 50mg
List of documents submitted	1. GMP certificate DE_NW_02_GMP_2019_0002 2. Manufacturing authorization DE_NW_02_MIA_2020_0001 3. Manufacturing protocols – secondary packaging/labelling for Deltyba 50 mg (Delamanid Tablet, Film-coated 50mg) 4. List of regulatory authority inspections 5. PQR Deltyba 50 mg x 48 tablets (2018 & 2019) 6. SMF 7. GMP inspection report Detmold District Council, 2017 8. CAPAs to the GMP inspection report Detmold District Council, 2017 9. GMP inspection report Detmold District Council, 2019 10. GMP inspection report Detmold District Council, 2019 11. Memo Out of stock situation 12. Memo Warning letters 13. Memo Self -inspection 14. Memo List of products packed on site 15. Memo Recalls 16. Master BPR`s
Any documents missing?	N/A

Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last) and comments**	
Bezirksregierung Detmold Leopoldstr. 15 32756 Detmold Germany	Dates of inspection:	18 – 19.06.2019
	Type of inspection:	GMP routine inspection
	Block/Unit:	Manufacturing areas 1, 2 and 3 Storage area
	Type of activities covered:	Secondary packaging
Bezirksregierung Detmold Leopoldstr. 15 32756 Detmold Germany	Dates of inspection:	21.06.2017
	Type of inspection:	GMP routine inspection
	Block/Unit:	Manufacturing areas 1, 2 and 3 Storage area
	Type of activities covered:	Secondary packaging
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**	
BPR	Batch production record	
GMP	Good manufacturing practices	
PQR	Product quality review	
SMF	Site Master File	
CAPA	Corrective actions and preventive action	

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

a) List of all regulatory inspections performed in the last 5 years and their outcomes:

Inspected authority	Date	Outcome
Bezirksregierung Detmold Leopoldstr. 15 32756 Detmold Germany	23. - 24.06.2015 (GMP inspection)	Complies
	20. - 21.06.2017 (GMP + GDP inspection)	Complies
	19.06.2019 (GMP + GDP inspection)	Complies

b) Manufacturing authorization granted by national authorities:
Manufacturing authorization DE_NW_02_MIA_2020_0001
GMP certificate DE_NW_02_GMP_2019_0002

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

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

- Oral solutions
- Powders for preparation of sterile solutions
- Hard gelatine capsules
- Soft gelatine capsules
- Sterile solutions
- Gels
- Eye drops
- Eye emulsions
- Tablets
- Surgical products

Therapeutic groups:

- Cholesterol treatment
- Various cancer treatment
- Blood coagulation factors
- Severe lung infections
- Antithrombin III deficiency
- Multiple sclerosis
- Dry eye syndrome
- Antithrombotics
- Cardiovasculars
- Antidepressants
- Mucoviscidosis
- Skin disease
- Bacterial inflammation

e) Most recent product quality review (PQR)of the concerned WHO product:
Submitted and reviewed for Deltyba 50 mg x 48 tablets (2018 & 2019)

f) Batch packaging records for the most recently released batch of relevant product:
Manufacturing protocols – secondary packaging/labelling for Deltyba 50 mg (Delamanid Tablet, Film-coated 50mg) submitted and reviewed

g) Master batch packaging records of the product of interest:
Master BPR`s submitted and reviewed

h) If any of the products are sterile, the completed batch records for the most recent media fill validation that is relevant to the products of interest and report on its outcome:
N/A

i) Recalls in the past three years related to products with quality defects:
Memo submitted: no recalls declared

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

k) 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:
Memo submitted: no warning letter, or equivalent regulatory action, issued by any authority

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

l) Additional documents submitted:
N/A

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 Arvato Distribution GmbH located at Gottlieb-Daimler-Strase 1, 33428 Harsewinkel, Germany** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines for 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-forth 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-forth 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-forth 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