World Health Organization

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Prequalification Unit Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Desk Assessment of Finished Product Manufacturer
(Manufacturer of Spray Dried Powder)

Part 1	**General information**
Company information	
Name of Manufacturer	Gohkakizawa Factory, Fuji Chemical Industries Co., Ltd
Corporate address of manufacturer	55 Yokohoonji, Kamiichi-machi, Nakaniikawa-gun, Toyama 930-0355, Japan +81-76-472-2323
Inspected site	
Name & address of manufacturing site	Fuji Chemical Industries Co., Ltd 1 Gohkakizawa, Kamiichi-machi, Nakaniikawa-gun, Toyama, 930-0405, Japan DUNS: 69-172-8950
Production Block/Unit	Building C28 Building C39
Desk assessment details	
Start and end dates of review	03 – 05 June 2020
Product covered by this desk assessment	Delamanid Tablet, Film-coated 50mg
List of documents submitted	1. SMF 2. List of regulatory inspections performed in the last 5 years and their outcomes 3. Pharmaceutical Policy Section, Health and Welfare Division, Toyama Prefectural Government Inspection reports (October 31 – November 2, 2017) and (4 – 7 February 2020) and CAPAs to inspection 4 – 7 February 2020 4. US Food and Drug Administration Establishment Inspection Report 5. Manufacturing authorization granted by national authority 6. List of all the products and dosage forms manufactured on-site 7. PQR Delamanid Spry Dried Powder, Jan – Dec 2019 8. Batch manufacturing and packaging records, including the analytical part, for: • In-process testing records for Lots XX and ZZ • Packaging and labelling inspection record for Lot XX • Production and control record for Lot XX • Release testing record for Lot XX • Release testing record for Lot XX particle size distribution 9. Master batch manufacturing and packaging records for: • Master in-process testing record • Master packaging and labeling inspection record • Master production and control record Delamanid spray dried powder • Master release testing record • Master spreadsheet of identification and assay • Master spreadsheet of Residual solvents 10. Declaration no recalls in the past three years related to products with quality defects 11. Declaration self-inspection has been performed, all matters dealt with 12. Declaration no warning letters

	Declaration no out-of-stock situations	
Part 2	**Summary of SRA/NRA inspection evidence considered**	
Pharmaceutical Policy Section, Health and Welfare Division, Toyama Prefectural Government Prefecture, Japan	Dates of inspection:	31 October, 1 – 2 November 2017
	Type of inspection:	Routine
	Block/Unit:	Buildings: • B6 • B8 • B18 • B20 • B21 • B22 • C14 • C15 • C17 • C18 • C24 • C25 • C30 • C41
	Type of products/Dosage forms covered:	• APIs • Tablets
US Food and Drug Administration	Dates of inspection:	12 – 16 March 2018
	Type of inspection:	Pre-Approval Inspection, Routine
	Block/Unit:	Buildings: • C44 • B18
	Type of products/Dosage forms covered:	• Spray-Dried Dispersion Powder • APIs
Pharmaceutical Policy Section, Health and Welfare Division, Toyama Prefectural Government	Dates of inspection:	4 – 6 February 2020
	Type of inspection:	Routine
	Block/Unit:	Buildings: • B6 • B20 • C14 • C15 • C17 • C39 used for production of Delamanid Spray Dried Powder • C18 • C27 • C28 used for production of Delamanid Spray Dried Powder • B18 • C10

	Type of products/Dosage forms covered:	• Spray Dried Powder • APIs • Tablets
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	The site has never been inspected by WHO	
Abbreviations	**Meaning**	
CAPA	Corrective and preventive action	
GMP	Good manufacturing practices	
FPP	Finished pharmaceutical product	
PQR	Product quality review	
PQR	Product quality review	
NAI	No actions indicated	
QRM	Quality risk management	
FPP	Finished pharmaceutical product	
API	Active pharmaceutical ingredient	
SMF	Site master file	
SOP	Standard operating procedure	

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

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

Regulatory Authority	Dates of inspection
Toyama Prefecture (Japan)	January 2016
TMMDA (Turkey)	January 2016
FDA (USA)	September 2016
PMDA (Japan)	November- December 2016
Toyama Prefecture (Japan)	October-November 2017
FDA (USA)	March 2018
CFDI (China)	January 2019
ANVISA (Brazil)	January 2019
Toyama Prefecture (Japan)	February 2020
Ministry of Industry and Trade of the Russian Federation (Russia)	February 2020

b) Manufacturing authorization granted by national authorities:
16AZ000291

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 manufactured on-site:

APIs: therapeutically groups:

- 28 APIs: Antacid, Anti-ulcer, Purgative, Functional-dyspepsia agent, Anti-virus, Cerebral vasodilator, Anti-allergic, Anti-cancer, Chronic pancreatitis agent, Antidysuria, Diabetic agent, Antihyperphosphatemic, Vitamin and Antifungal

Intermediates: therapeutically groups:

- 16 Intermediates: Antacid, Anti-ulcer, Purgative, Anti-virus, Anti-tuberculosis, Anti-allergic, Anti-hyperlipidemic and Elemental diet

FPPs – tablets: therapeutically groups:

- 9 Products: Anti-cancer, Erectile dysfunction drug, Androgenetic alopecia drug

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

PQR Delamanid Spry Dried Powder submitted and reviewed

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

Submitted and reviewed for Delamanid Spry Dried Powder:

- In-process testing records for Lots XX
- Packaging and labelling inspection record for Lot XX
- Production and control record for Lot XX
- Release testing record for Lot XX
- Release testing record for Lot XX particle size distribution

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

- Master in-process testing record Delamanid Spry Dried Powder
- Master packaging and labeling inspection record Delamanid Spry Dried Powder
- Master production and control record Delamanid spray dried powder
- Master release testing record Delamanid Spry Dried Powder
- Master spreadsheet of identification and assay Delamanid Spry Dried Powder
- Master spreadsheet of Residual solvents Delamanid Spry Dried Powder

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

N/A

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

Declaration submitted: no recalls

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:

Declaration submitted: self-inspection has been performed, 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:
Declaration submitted: no warning letters

k) Out-of-stock situations:
Declaration 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 ***Gohkakizawa Fuji Chemical Industries Co., Ltd,*** located at ***1 Gohkakizawa Kamiichi-machi, Nakaniikawa-gun, Toyama, 930-0405, Japan*** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines for purposes of spray dried powder.

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. Forty-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