World Health Organization

20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

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	Minsheng Group Shaoxing Pharmaceutical Co., Ltd.
Corporate address of manufacturer	315 Tanggong Rd, Paojiang Industrial Zone, Shaoxing City, 312071 Zhejiang Province, China Telephone Number: 86-575-88912706 Fax Number: 86-575-88912706 Email Address: mssxyy@mspharm.com 24 hrs Telephone Number: 86-575-88912702/86-13777320639
Inspected site	
Name & address of manufacturing site	Minsheng Group Shaoxing Pharmaceutical Co., Ltd. 315 Tanggong Rd, Paojiang Industrial Zone, Shaoxing City, 312071, Zhejiang Province, China DUNS No. 544607919
Synthetic Unit/Block/Workshop	Workshop 102
Desk assessment details	
Date of review	19 September 2019 to 28 October 2019
APIs covered by this desk assessment	Praziquantel
List of documents submitted	• Certificate of certified translator. • List of regulatory inspections performed at the site during the last 5 years. • List of full inspection report(s), inspection reports, CAPA reports and final decisions by the regulatory authority (including US FDA, EDQM, PMDA etc.). • Manufacturing license, Certificate No. Zhe20040270 issued on the 22/11/2018 by Zhejiang Food and Drug Administration. • Site Master File, effective date 1.4.2019. • list of all the products manufactured on-site. • The APQR report for Praziquantel (Process B). • Completed BMRs for Praziquantel. • Blank BMRs for Praziquantel. • Declaration on product *XXX* Recall. • Self-inspection report of Praziquantel issued on 3/4/2019.

	• A warning letter statement: There is no copy of any warning letter, or equivalent regulatory action, issued by any authority to which the site provides or has applied to provide any APIs manufactured at the site. • A statement: Minsheng did not have any the out-of-stock situation during the past 3 years.	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last)**	
US Food and Drug Administration (US FDA)	Dates of inspection:	21-25. January 2019
	Type of inspection:	Pre-approval inspection
	Block/Unit/Workshop:	Workshop 102 Workshop 103 Workshop 104 Workshop 105
	Type of APIs covered:	APIs manufactured by chemical synthesis
Austrian federal Office for Safety in Health Care (AGES)	Dates of inspection:	2-5 July 2018
	Type of inspection:	Routine Inspection
	Block/Unit/Workshop:	Workshop 101
	Type of APIs covered:	APIs manufactured by chemical synthesis
EDQM	Dates of inspection:	19-21 April 2018
	Type of inspection:	Pre-approval inspections for Atropine Sulfate
	Block/Unit/Workshop:	Workshop 103
	Type of APIs covered:	APIs manufactured by chemical synthesis
Pharmaceuticals and Medical Devices Agency (PMDA)	Dates of inspection:	17-19 January 2018
	Type of inspection:	Not mentioned
	Block/Unit/Workshop:	Workshop 101
	Type of APIs covered:	APIs manufactured by chemical synthesis
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	The inspection of Minsheng Group Shaoxing Pharmaceutical Co., Ltd. was last performed by WHO PQT on 9~12/1/2017. This was the 3rd inspection of this site. It was found compliant with only 4 major deficiencies and 19 listed as Other.	
Brief description of manufacturing activities	Production, quality control, packaging, storage and distribution of APIs. At the site about 30 APIs and intermediates were manufactured. According to the company no penicillin, cephalosporins were manufactured on this site.	
General information about the company and manufacturing site	The company covers an area of 233330m^2, with building area of 56467m^2. It has five workshops for APIs, Quality Unit, Power Workshop, Machine Repair Workshop, a variety of Warehouses, Waste treatment and other ancillary facilities.	

Focus of the last WHO inspection	The production of PQT API from intermediate Benzoyl-Praziquantel (Cyclidehydrate) took place in 4 steps with two different processes for PQT USP and Chinese Pharmacopoeia (CP) grades. Processing was conducted according to the instructions in the BMR.
Areas inspected	• Quality management system • Manufacturing areas in Workshop 102 including chemical reaction area and grade D area for final stage. • QC laboratory • Warehouse raw materials and finished API products
Out of scope and restrictions (last WHO inspection)	None
WHO APIs covered by the last WHO inspection	Praziquantel (APIMF301)
Additional products covered by this desk assessment:	None
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:

- Manufacturing license, Certificate No. Zhe20040270, Issued: 22/11/ 2018 by Zhejiang Food and Drug Administration.
- GMP Certificate was not submitted.

b) Site master file (SMF):

Site master file, effective date 1.4.2019 was reviewed and found acceptable and in line with the WHO TRS No. 961, Annex 14.

c) List of all the APIs or other products (intermediates, dosage forms) manufactured on-site:

List: N(2)-L-Alanyl-L-Glutamine, Mecobalamin, Emamectin Benzoate, Florfenicol, Flunixin Meglumine, Praziquantel, Netobimin, Fluconazole, Raceanisodamine, Spironolactone, Atropine Sulfate(Atropine Sulphate), Tropine, Cetylpyridinium Chloride, Tropisetron Hydrochloride, Fursultiamine Hydrochloride, Fursultiamine, Alendronate Sodium, Tropicamide, Hydruobenzole Hydrochloride, Homoharringtonine, Vindesine Sulfate, Vinorelbine Tartrate, Riboflavin Sodium Phosphate, Pyrantel Pamoate (Pyrantel Embonate), Pyrantel Tartrate, Morantel Tartrate, Morantel Citrate, Oxantel Pamoate, Furazolidone.

The facility manufactures highly potent substances in workshop 104 and/or 105, such as Vindesine, Vinorelbine, Homoharringtonine (cytostatics).

d) List of all regulatory inspections performed in the last 3 years and their outcomes:

• US FDA inspection in 21-25/1/2019 compliant (According to the response of the company, no inspection report and certificate provided).
• CFDA inspection in 17-19/9/2018 compliant.
• AGES inspection in 2-5/7/2018 compliant.
• EDQM inspection in 19-21/4/2018 compliant.
• PMDA inspection in 17-19/1/2018 compliant.
• US FDA inspection in 19-14/4/2017 compliant.
• CFDA inspection in 11-14/3/2017 compliant.
• WHO inspection in 9-12/1/2017 compliant.

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

The APQR report for Praziquantel (Process B). It shows that there was only one batch of reprocess Praziquantel (Process B) was manufactured in year 2018(442.3kg), the product quality complies with specification, product stability test results comply with corresponding specification.

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

Praziquantel Batch Manufacture Records (Executed, Batch No. PQT*XXX*).
Praziquantel QC analysis data Records (Executed, Batch No. PQT*XXX*).

g) Master batch manufacturing and packaging record(s) of the API(s) of interest:
Blank master batch manufacturing records of the Praziquantel (Process B) were submitted.

h) Recalls in the past three years related to APIs with quality defects:
Declaration on *XXX* Recall: The recall of *XXX* was caused by deficiency found in WHO inspection in May 2015. There was no recall related with Praziquantel API in Shaoxing Minsheng.

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:
Self-inspection report of Praziquantel issued on 3/4/2019.

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):
A warning letter statement: There is no copy of any warning letter, or equivalent regulatory action, issued by any authority to which the site provides or has applied to provide any APIs manufactured at the site.

k) Out-of-stock situations:
A statement confirming that no out-of-stock situation in the past 3 years.

l) Additional documents submitted:
None.

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 ***Minsheng Group Shaoxing Pharmaceutical Co., Ltd.*** located at ***315 Tanggong Rd, Paojiang Industrial Zone, Shaoxing City, Zhejiang Province, China*** 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

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-eighth 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*. 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/

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. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Fifty-third Report Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 2. **Short name: WHO TRS No. 1019, Annex 2**
   https://apps.who.int/iris/bitstream/handle/10665/312316/9789241210287-eng.pdf?ua=1

7. Good manufacturing practices: guidelines on validation. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Fifty-third Report Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 3. **Short name: WHO TRS No. 1019, Annex 3**
https://apps.who.int/iris/bitstream/handle/10665/312316/9789241210287-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. 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 3.
Short name: WHO TRS No. 957, Annex 3
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*. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 5.
Short name: WHO TRS No. 996, Annex 5
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.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. 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 TRS No. 996, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

24. 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