World Health Organization

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

Part 1	**General information**
Company information	
Name of Manufacturer	Solara Active Pharma Sciences Limited
Corporate address of manufacturer	Solara Active Pharma Sciences Limited Batra Centre No. 28, Sardar Patel Road. Post Box 2630 Guindy, Chennai- 600 032, India
Inspected site	
Name & address of manufacturing site	Solara Active Pharma Sciences Limited A 1 /B SIPCOT Industrial Complex, Kudikadu Village, Cuddalore 607005, Tamil Nadu, India.
Desk assessment details	
Date of review	01-05 April and 21-25 June 2021
APIs covered by this desk assessment	WHOAPI-177 Cycloserine WHOAPI-236 Tenofovir disoproxil fumarate
List of documents submitted	1. A copy of the manufacturing authorization. 2. The most recent version of the SMF, including legible printouts of the water system and HVAC system (i.e. clean areas for processing APIs), including pipeline and instrumentation drawings. 3. A list of all the APIs (medicinal or other) manufactured on site. Please indicate the buildings for the manufacture of WHO PQ APIs and if there are any shared facilities and equipment for these APIs. 4. Copies of inspection reports by a stringent regulatory authority completed in the last two years. 5. CAPAs and proof of CAPAs implementation related to the above-mentioned inspection reports. 6. A copy of the procedure on batch codification. 7. A list of solvents being recovered, the relevant procedure and controls on recovered solvents. 8. A copy of any warning letter or equivalent regulatory action issued by any authority to which the site provides or has applied to provide a product. 9. The most recent PQRs of WHO PQ APIs. 10. A confirmation by the senior QA representative that a full self-inspection or external audit dedicated to prequalified APIs has been performed and all matters dealt with 11. A list of any recalls carried out in the last 3 years

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	12. Master batch manufacturing records of WHO PQ APIs as well as one completed BMR corresponding the latest production of each of the above-mentioned APIs	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last)**	
USFDA, USA	Dates of inspection:	01-05.07.2019
	Type of inspection:	Post-approval
	Block/Unit/Workshop:	N/A
	Type of APIs covered:	Gabapentin USP Sevelamer carbonate
USFDA, USA	Dates of inspection:	17-21.04.2017
	Type of inspection:	Pre-approval
	Block/Unit/Workshop:	N/A
	Type of APIs covered:	Potassium Citrate (assay test) Ranitidine Mirabegron Sevelamer Carbonate Cycloserine Gabapentin Nizatidine Olanzapine Methohexital
PMDA, Japan	Dates of inspection:	07-09.03.2017
	Type of inspection:	Routine inspection
	Block/Unit/Workshop:	N/A
	Type of APIs covered:	Nizatidine
EDQM *MHRA, UK*	Dates of inspection:	09-11.01.2017
	Type of inspection:	Routine inspection
	Block/Unit/Workshop:	PBII, PBIII, PBIV
	Type of APIs covered:	Olanzapine, Nabumetone, Nizatidine, Gabapentin, Ranitidine, Venlafaxine
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	The last on-site inspection was carried out during 24-26 October 2016 and it concluded that a follow up inspection had to be carried out. The follow up inspection was carried out in the form of desk assessment in May 2017 and the site was found to be compliant with WHO GMP	
Brief description of manufacturing activities	Manufacture including production, quality control and release of non-beta lactam and non-penicillin group: • Active Pharmaceutical Ingredients and intermediates	

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General information about the company and manufacturing site	Shasun Pharmaceuticals Limited was established in 1976. The firm set up its plant at Cuddalore, Tamil Nadu, India in the year 1991 to manufacture Active Pharmaceuticals Ingredients and their intermediates. This Cuddalore API site is situated at A1/B, SIPCOT Industrial Complex, in Kudikadu village, Cuddalore - 607005, which is about 180 km away from Chennai, the capital of Tamil Nadu state (India). This site is a multiproduct facility manufacturing APIs and their intermediates for different Regulatory markets. This API site has been inspected by several Regulatory Authorities.
Focus of the last WHO inspection	Follow up inspection
Areas inspected	Pharmaceutical Quality System Production System Facilities and Equipment System Laboratory Control System Materials System
Out of scope and restrictions (last WHO inspection)	Packaging and Labeling System and microbiological laboratory
WHO APIs covered by the last WHO inspection	• APIMF 177 Cycloserine (used for TB222 Cycloserine Capsules, hard 250mg) • APIMF 236 Tenofovir disoproxil (fumarate)

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

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Part 4	Summary of the assessment of supporting documentation

a) Manufacturing authorization and GMP certificate granted by the local authority:
Valid manufacturing license and GMP certificates were provided in support of the manufacturing activities on-site.

b) Site master file (SMF):
The company provided the latest version of the SMF. It is noted that the revision history of the SMF includes two versions coded as R0. The change control for these revisions should be checked at the next inspection.
Shasun Chemicals and Drugs Limited was established in 1976, in Chennai. The company set up its second API plant at Cuddalore, Tamil Nadu, India, in 1991. In 2015 Shasun Pharmaceuticals Limited merged with Strides Arcolab Limited and created Strides Shasun Limited. Further to that, in 2018 it was decided to separate API manufacturing from other Strides Shasun Ltd operations and activities and a new business entity, Solara Active Pharma Sciences Ltd. was formed.
The manufacturing site in Cuddalore consists of 5 production blocks (PB), 13 packing sections (PS), a dedicated laboratory and a pilot plant.
Cycloserine is manufactured and packaged at PB-IV and PS-V. Tenofovir disoproxil fumarate is manufactured and packaged at PB-III and PS-VII. Premises and equipment are not dedicated for these APIs.

c) List of all the APIs or other products (intermediates, dosage forms) manufactured on-site:
The company provided a list of 39 APIs that have been manufactured on site the last 5 years. According to the manufacturing license the site is authorized to manufacture 115 APIs of different grades and specifications, for the domestic market and export.

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

Regulatory Authority	Inspection date	Outcome
USFDA, USA	02-07.05.2020	Pending EIR
USFDA, USA	01-05.07.2019	GMP compliant
USFDA, USA	17-21.04.2017	GMP compliant
PMDA, Japan	07-09.03.2017	GMP compliant
Joint EDQM – MHRA, UK	09-11.01.2017	GMP compliant

e) Most recent product quality review(s) (PQR)(s) of the concerned WHO API(s):
A PQR for Tenofovir disoproxil fumarate was not provided. According to the company no batches of this API were manufactured in the last 6 years.
The 2021 PQR(batches manufactured in 2020) for Cycloserine was provided. The PQR includes a review for each production stage, materials used, suppliers, validations, equipment and facilities qualification, stability studies, deviations, OOS, complaints, recalls, returns and rejections.
Trending of critical quality attributes and specifications was performed and it is included in the report.

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

The company provided the most recent completed BMR for Cycloserine which did not give rise to any comments.

No completed BMR for Tenofovir disoproxil fumarate was provided since no bathes have been manufactured in the last six years

g) Master batch manufacturing and packaging record(s) of the API(s) of interest:

Master BMRs for Cycloserine and Tenofovir disoproxil fumarate were provided.

h) Recalls in the past three years related to APIs with quality defects:

No recalls have been carried out in the last three years according to the company's declaration

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:

According to the company the self-inspection programme is conducted in accordance with Solara's corporate quality system procedure on "internal audit program". Software is used for planning, recording audit reports, approval of audit responses, CAPA implementation and closure. Self-inspection is carried out twice per year and covers all six systems of PQS. WHO PQ products are covered during self-inspection.

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):

No warning letter or any other equivalent regulatory action has been taken against the site.

k) Out-of-stock situations:

No out of stock situations have been experienced and no such situations are foreseen for the near future

l) Additional documents submitted

The following documents and procedures were provided, reviewed and did not give rise to any comments:

Blueprints of water system and HVAC system

Batch codification procedure

Declaration on not contracting any third party or performing for any third party recovery of solvents.

Procedure on solvent recovery

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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 ***Solara Active Pharma Sciences Limited*** located at ***A 1 /B SIPCOT Industrial Complex, Kudikadu Village, Cuddalore 607005, Tamil Nadu, India*** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines for APIs.
This compliance status shall be valid until **July 2022** or when another inspection is conducted by WHO or by a stringent regulatory authority.

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 WHO 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 TRS No. 986, Annex 2***
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/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. 961, 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. WHO Recommendations for quality requirements when plant – derived artemisin is used as a starting material in the production 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

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 GDRMP guidance or 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. 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

23. 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

24. 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

25. 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

26. 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

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27. 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

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