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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	**ST Pharm Co. Ltd. (Banwol site)**
Corporate address of manufacturer	ST Pharm Co. Ltd. - Banwol Site, 171, Haean-ro, Danwon-gu Ansan-si, Gyeonggi-do 15610 Republic of Korea
Inspected site	
Name & address of manufacturing site	ST Pharm Co. Ltd. - Banwol Site, 171, Haean-ro, Danwon-gu Ansan-si, Gyeonggi-do 15610 Republic of Korea
Synthetic Unit/Block/ Workshop	Plant A Sector 2 and Plant C
Desk assessment details	
Date of review	14-16 June 2023 27-29 September 2023 21-23 November 2023
APIs covered by this desk assessment	Cycloserine Cycloserine Terizidone
List of documents submitted	The following documents were provided: 1. List of regulatory inspections 2. Inspection report USFDA 3. CAPA 4. Manufacturing Authorization and GMP Certificate 5. Site Master File 6. Lay outs of the facilities 7. List of products manufactured on-site 8. 2022 Cycloserine PQR 9. 2021 Terizidone PQR 10. BMR, BPR and Analytical Record of Cycloserine 11. BMR, BPR and Analytical Record of Terizidone 12. List of recalls 13. Declaration of GMP 14. Master BMR and BPR of Cycloserine 15. Master BMR and BPR of Terizidone

	16. Waste management practices 17. Declaration for non-compliance 18. Declaration for out-of-stock situations 19. List of upcoming inspections 20. Manufacturing process covered by the USFDA inspection	
Part 2	**Summary of SRA/NRA inspection evidence considered**	
USFDA	Dates of inspection:	16-20.05.2022
	Type of inspection:	Pre-approval inspection
	Block/Unit/Workshop:	Oligo-Plant
	Type of APIs covered:	APIs for hyperlipidemia and contrast agents
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	18 November 2016 (Routine). GMP compliant 28 October 2020 Desk assessment. GMP compliant	
Brief description of manufacturing activities	Manufacturing, packaging, quality control, stability testing and storage of small chemical molecules and oligonucleotides.	
General information about the company and manufacturing site	ST Pharm Co., Ltd is a member of Dong-A Socio Group. The company was originally called Samschully Pharm and was established in 1983. In 2010, the company joined Dong-A Socio Group and changed name to ST Pharm. ST Pharm consists of two manufacturing sites located in Sihwa and Banwol. The Banwol campus originally consisted of two sites namely Banwol site 1 (Section 1/2/3/4 and warehouse) and Banwol site 2 (Plant 1/2/3). Additionally, the Oligo-Plant came into operation since the last desk assessment. The previous desk assessment suggests that the company wanted to manufacture Terizidone and Cycloserine in Plant A. However, the 2021 Terizidone PQR suggest that during the review period the Terizidone API was manufactured in Plant C and Plant A Sector 2.	
Focus of the last WHO inspection	Non-sterile APIs manufactured by chemical synthesis	
Areas inspected	In 2016, Banwol 2: Synthesis Plant 2 was only covered, with a focus on the Cycloserine API. Warehousing, quality control and other ancillary areas were covered. Plants 1 and 3, also located at Banwol 2, were not covered.	
Out of scope and restrictions	N/A	

(last WHO inspection)	
WHO APIs covered by the last WHO inspection /desk assessment	Cycloserine Terizidone
Additional products covered by this desk assessment:	N/A
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:
The company provided the most recent Certificate of Pharmaceutical Manufacturing License and the original Manufacturing Authorization, as well as the most recent GMP certificate which was issued in May 2021

b) Site master file (SMF):
The most recent version of the SMF was provided. The document included a brief description of the QMS system and the GMP operations on site. The SMF was complimented by 9 Annexes including the manufacturing authorization, the most recent GMP certificate, the import license, the list of APIs

manufactured on site, the company's organization chart, the layouts of the facilities, the water system and the list of equipment.

c) List of all the APIs or other products (intermediates, dosage forms) manufactured on-site:
The list of 18 APIs manufactured on-site was provided. No beta lactams or any other highly sensitizing material are manufactured on-site. It is noted that Appendix 4 of the SMF includes a few different APIs manufactured on-site.

d) List of all regulatory inspections performed in the last 3 years and their outcomes:
The company provided an overview of the authorities that had inspected the site in the last 5 years.

Date	Authority	Result
13-16 Aug. 2018	MFDS	Approved
25-27 May 2021	MFDS	Approved
16-20 May 2022	U.S.FDA	Approved

It is noted that the site has also been inspected by PMDA but the exact issue date of the GMP certificate in the SMF is not clear.
The site had not been informed of any upcoming regulatory inspections at the time they submitted the documentation for this desk assessment.

e) Most recent product quality review(s) (PQR)(s) of the concerned WHO API(s):
The 2021 Terizidone PQR was provided. 15 batches were manufactured during the review period. All batches met the specifications. No anomaly was detected in process controls. No deviations were registered. No OOS/OOT results were recorded. One complaint was registered, investigated, and closed out. One return was also registered. No recall was carried out during the review period. Recommendations from the previous PQR were followed up and implemented.
The company also provided the 2022 Cycloserine PQR. 32 batches were manufactured during the review period, and all met the established specifications. IPC test results were also found within the set limits. No OOS results were detected. No reprocessing/reworking occurred. Two deviations were registered, investigated, and closed out. No complaints, recalls or returns were registered during the review period.

f) Batch manufacturing and packaging record(s), including the analytical part, for the most recently released batch of relevant API(s):
The company provided a recently completed Cycloserine BMR/BPR and the relevant analytical record. Similarly, the latest Terizidone BMR/BPR and the relevant analytical record were also shared. Certain parts of the BMRs (e.g., Batch record checklist) had not been translated to English and could not be followed and reviewed.

g) Master batch manufacturing and packaging record(s) of the API(s) of interest:
The company provided translated versions of the Master BMR/BPR of Terizidone and Cycloserine APIs. Review of these documents did not give rise to any comments.

h) Recalls in the past three years related to APIs with quality defects:
The company confirmed that no recall of Terizidone or Cycloserine had occurred in the last three years

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:

The company confirmed that an internal system for self-inspections was in place and covered all GMP aspects and products

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 equivalent non-compliance notification has been issued for the site or the APIs

k) Out-of-stock situations:

No out-of-stock situation in relation to Terizidone and Cycloserine has occurred

l) Additional documents submitted:

The company provided responses to three questions related to waste management. More specifically, the company provided details on waste disposal of Cycloserine residues, and intermediates. Waste disposal is contracted out and meets the requirements of the Korean government. It is not clear if the company is aware of the "Points to consider for manufacturers and inspectors: environmental aspects of manufacturing for the prevention of antimicrobial resistance" (WHO TRS1025, Annex 6) and has conducted the relevant risk assessment. This issue should be discussed during the next inspection. Additionally, the company provided layouts of the facilities and the P&ID of the water system.

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 ***ST Pharm Co. Ltd, Banwol*** located at ***171, Haean-ro, Danwon-gu, Ansan-si, Gyeonggi-do, 15610, Republic of Korea*** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines for APIs.

This WHOPIR will remain valid until 21.11.2025, provided that the outcome of any inspection conducted during this period is positive.

Part 6	**List of guidelines referenced in this inspection report**

1. 1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eight Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2.
   Short name: WHO TRS No. 986, Annex 2
   https://www.who.int/publications/m/item/trs986-annex2

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

https://www.who.int/publications/m/item/annex-2-trs-957

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/publications/m/item/trs1010-annex9

4. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 3.
   Short name: WHO TRS No. 1033, Annex 3
   https://www.who.int/publications/m/item/annex-3-trs-1033

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
   https://www.who.int/publications/m/item/annex-4-trs-929

6. WHO good practices for pharmaceutical quality control laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-seventh Report. Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052), Annex 4.
   Short name: WHO TRS No. 1052, Annex 4
   https://www.who.int/publications/i/item/9789240091030

7. 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
   https://www.who.int/publications/m/item/trs957-annex3

8. 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
   https://www.who.int/publications/m/item/Annex-8-trs-1010

9. 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, 2018 (WHO Technical Report Series, No. 1019), Annex 2.

Short name: WHO TRS No. 1019, Annex 2
https://www.who.int/publications/m/item/trs1019-annex2

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
Short name: WHO TRS No. 1044, Annex 4
https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/production/trs1044-annex4-technology-transfer-in-pharmaceutical-manufacturing.pdf

11. WHO good manufacturing practices for sterile pharmaceutical products. Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
Short name: WHO TRS No. 1044, Annex 2
https://www.who.int/publications/m/item/trs1044-annex2

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***
https://www.who.int/publications/m/item/trs943-annex3

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
https://www.who.int/publications/m/item/trs961-annex2

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
https://www.who.int/publications/m/item/trs981-annex2

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
https://www.who.int/publications/m/item/annex-3-trs-981

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
https://www.who.int/publications/m/item/tr961-annex14

17. 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://www.who.int/publications/m/item/trs1019-annex3

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
https://www.who.int/publications/m/item/trs992-annex4

19. 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
https://www.who.int/publications/m/item/trs961-annex9-modelguidanceforstoragetransport

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
https://www.who.int/publications/m/item/trs992-annex5

21. WHO Recommendations for quality requirements when plant – derived artemisinin 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
https://www.who.int/publications/m/item/trs-992-annex-6

22. Guideline on data integrity. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 4.
Short name: WHO TRS No. 1033, Annex 4
https://www.who.int/publications/m/item/annex-4-trs-1033

23. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10.
Short name: WHO TRS No. 996, Annex 10
https://www.who.int/publications/m/item/trs966-annex10

24. 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***
https://www.who.int/publications/m/item/trs1010-annex10

25. Points to consider when including Health-Based Exposure Limits in cleaning validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 2.
Short name: WHO TRS No. 1033, Annex 2
https://www.who.int/publications/m/item/annex-2-trs-1033

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/m/item/trs-1025-annex-6

27. 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/m/item/trs-1025-annex-3-water-for-injection

27. 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/m/item/trs1025-annex4

28. Good trade and distribution practices for pharmaceutical starting materials. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 6.
Short name: WHO TRS No. 996, Annex 6
https://www.who.int/publications/m/item/annex-6-trs-996

29. WHO guidelines for preparing a laboratory information file. *WHO Expert Committee on Specifications for Pharmaceutical Preparations.* Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 13.
Short name: WHO TRS No. 961, Annex 13
https://www.who.int/publications/m/item/trs961-annex13

30. WHO good manufacturing practices for excipients used in pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-seventh Report. Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052), Annex 1.
Short name: WHO TRS No. 1052, Annex 1
https://www.who.int/publications/i/item/9789240091030