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	Laurus Labs Limited (Unit-4)
Corporate address of manufacturer	2nd Floor Serene Chambers, Road No.:7 Banjara Hills, Telangana Hyderabad, 500 034 India Phone No.: +91-40-39804333 Website: www.lauruslabs.com
Inspected site	
Name & address of manufacturing site	Laurus Labs Limited (Unit-4) Plot No 25, 25A to 25K, APSEZ – De-Notified area, Lalamkoduru Village, Rambilli Mandal, Visakhapatnam – 531011, Andhra Pradesh, India Latitude N 17° 32' Longitude E 80° 0'
Synthetic Unit/Block/Workshop	Manufacturing Block 6A (MB-6A)
Desk assessment details	
Start and end dates of review	10 – 13 August 2020
APIs covered by this desk assessment	Lopinavir
List of documents submitted	1. GMP certificate 2. Manufacturing authorization license No.20/VSP/AP/2017/B/G 3. SMF 4. PQR Lopinavir (ALVR) August 2019 – July 2020 5. Analytical raw data ALVR-1 batch No XX 6. Analytical raw data ALVR-2 batch No XX 7. Analytical raw data ALVR-3 batch No XX 8. Analytical raw data Lopinavir batch No XX 9. Batch production and control record ALVR-1 batch No XX 10. Batch production and control record ALVR-2 batch No XX 11. Batch production and control record ALVR-3 batch No XX 12. Batch production and control record for packaging/repackaging Lopinavir batch No XX 13. Master Batch production and control record ALVR-1 14. Master Batch production and control record ALVR-2 15. Master Batch production and control record ALVR-3 16. Master Batch production and control record for packaging/repackaging 17. Declaration: forecast modification of facility at Unit-4

	18. List of regulatory GMP inspections 19. List of products manufactured at site 20. USFDA EIR 21. USFDA E mail XX Declaration: no deficiencies were noted during SRA inspection 22. Declaration: Sartan API process 23. Declaration: notification of upcoming inspections 24. Declaration: self-inspection 25. Declaration: recalls 26. Declaration: warning letters 27. Product inspection status by competent SRA	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last) and comments**	
USFDA	Dates of inspection:	8 – 12 July 2019
	Type of inspection:	cGMP inspection
	Block/Unit/Workshop:	Manufacturing Block 6A (MB-6A) / Manufacturing Block 6B (MB-6B)
	APIs covered:	• Lopinavir • Digoxin
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**	
MBPCR	Master Batch Production & Control Record	
BPCR	Batch Production & Control Record	
cGMP	Current Good manufacturing practices	
SRA	Stringent Regulatory Agency	
PQR	Product Quality Review	
EIR	Establishment Inspection Report	

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

a) Manufacturing authorization and GMP certificate granted by the local authority:
GMP certificate, dated 30-01.2020 No Rc.No.59/DD/DCA/VSP/2020, issued by Drugs Control Administration, Visakhapatnam Region
Manufacturing authorization license No.20/VSP/AP/2017/B/G

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

c) List of all the APIs or other products manufactured on-site:

Name of the Product	International Non-Proprietary Name (INN)	Therapeutic Category
Lopinavir	Lopinavir	Antiretroviral
Vildagliptin	Vildagliptin	Anti-diabetic; Dipeptidyl Peptidase IV Inhibitors
Sitagliptin Phosphate Monohydrate	Sitagliptin Phosphate Monohydrate	Dipeptidyl peptidase-4 (DPP-4) inhibitor, for the treatment of type-2 diabetes rnellitus
Sitagliptin Hydrochloride Monohydrate	Sitagliptin Hydrochloride Monohydrate	Dipeptidyl peptidase-4 (DPP-4) inhibitor, for the treatment of type-2 diabetes rnellitus Key starting material of Drug substance Raw material of Drug substance
Epoxide	Epoxide	
5-Chloro-2- pentanone (ACPT)	5-Chloro-2-pentanone	
Digoxin	Digoxin	Anti-arrhythmic
Etoricoxib	Etoricoxib	Analgesic, antipyretic and anti-inflammatory agent Non-steroidal anti- inflammatory drug, NSAI D Cyclo-oxygenase 2 (COX-2) inhibitor
Clopidogrel Hydrochloride	Clopidogrel Hydrochloride	Platelet aggregation inhibitor
Sitagliptin	Sitagliptin	Dipeptidyl peptidase-4 (DPP-4) inhibitor, for the treatment of type-2 diabetes mellitus
Rosuvastatin (RSCPZ)	Rosuvastatin (RSCPZ)	Intermediate of Rosuvastatin Calcium
Synoxyl HSS		
Bakuchiol		

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

Name of the Regulatory Agency	Dates of inspection	Outcome
Ma Consultores (on behalf of Mexican Agency)	14 – 15 December 2018	cGMP certificate issued
USFDA	8 - 12 July 2019	EIR Received

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

Submitted and reviewed:

- PQR Lopinavir August 2019 – July 2020

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

Submitted and reviewed:

- Batch production and control record ALVR-1 batch No XX
- Batch production and control record ALVR-2 batch No XX
- Batch production and control record ALVR-3 batch No XX
- Batch production and control record for packaging/repackaging Lopinavir batch No XX
- Analytical raw data ALVR-1 batch No XX
- Analytical raw data ALVR-2 batch No XX
- Analytical raw data ALVR-3 batch No XX
- Analytical raw data Lopinavir batch No XX

g) Master batch manufacturing and packaging records of the API of interest:

Submitted and reviewed:

- Master Batch production and control record ALVR-1
- Master Batch production and control record ALVR-2
- Master Batch production and control record ALVR-3
- Master Batch production and control record for packaging/repackaging

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

Declaration submitted: there are no recalls related to any of the Drug Substances manufactured at the site

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

Declaration submitted: self- inspections have been performed as per Quality System, SOP#QA/010 titled "Handling of self-inspections". Self- inspections are handled electronically using the electronic Quality Assurance Management (eQAMS) software. The frequency of the self-inspection is once in every four months i.e. thrice in a year by qualified cross functional team.

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):

Declaration submitted: no warning letters and/or Regulatory Action letters has been issued

k) Out-of-stock situations:

Declaration submitted: no out-of-stock situations has been encountered or is foreseen in near future

l) Additional documents submitted:

Declaration: Sartan API process: No Sartan products are being manufactured at the site
Declaration: no notifications of Inspections received from competent regulatory authorities for inspections in near future.

Part 5	Conclusion – Desk assessment outcome

Based on GMP evidence received and reviewed, it is considered that a desk assessment is acceptable in lieu of a WHO onsite inspection. The site ***Laurus Labs Limited (Unit-4, Manufacturing Block 6A - MB-6A),*** located at ***Plot No 25, 25A to 25K, APSEZ – De-Notified area, Lalamkoduru Village, Rambilli Mandal, Visakhapatnam – 531011, Andhra Pradesh, India*** 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 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. 1015), 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

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