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

Part 1	**General information**
Company information	
Name of Manufacturer	Honour Lab Limited
Corporate address of manufacturer	Honour Lab Limited H.NO.8-3-166/7/1 Erragadda, Hyderabad – 500018, Telangana – 502313, India www.honourlab.com
Inspected site	
Name & address of manufacturing site	Honour Lab Limited, Unit III Plot 4, Hetero Infrastructure Ltd., SEZ, N. Narasapuram Village, Nakkapally, Visakhapatnam, Andhra Pradesh, 531081 India Latitude: 17°22' 5 8"N Longitude: 82°43'32"E
Synthetic Unit/Block/Workshop	Block A, manufacturing section VII
Manufacturing license number	26/VP/AP/2013/B/R, valid up to 29.08.2023
Desk assessment details	
Start and end dates of review	21, 28 – 30 August 2020
API covered by this desk assessment	Remdesivir
List of documents submitted	1. USFDA EIR, dates of inspection 11 – 15 November 2019 2. FDA Form 483 3. CAPAs to Form 483 and response letter 4. List of regulatory inspections 5. OGYEI (Hungary) inspection report 6. CAPAs to OGYEI inspection report 7. OGYEI GMP certificate 8. Ministry of Industry and Trade of Russian Federation GMP certificate 9. Manufacturing license 10. Government of Andhra Pradesh Drugs Control Administration GMP certificate 11. SMF and layouts 12. List of products manufactured at site 13. PQR Clobazam 14. BMR/BPRs 15. Analytical raw data (intermediate) No XX 16. Analytical raw data (intermediate) No YY 17. Analytical raw data (finished API) No ZZ

	18. Declaration: recalls 19. Declaration: self-inspection 20. Declaration: warning letter 21. Master batch record – drying, micro-pulverization, sifting and packaging 22. Master batch record – stage I 23. Master batch record – stage II 24. Master batch record – stage III (finished API) 25. Facilities/equipment covered by SRA inspections 26. SOP "Preparation of Annual product quality review"	
Any documents missing?	N/A	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last) and comments**	
USFDA	Dates of inspection:	11 – 15 November 2019
	Type of inspection:	Surveillance and preapproval inspection
	Block/Unit/Workshop:	Block A, B and C
	APIs covered:	• Sacubitril Valsartan Sodium on Colloidal Silicon Dioxide WHO API was not specifically covered
OGYEI (Hungary)	Dates of inspection:	20 – 27 November 2019
	Type of inspection:	GMP compliance inspection
	Block/Unit/Workshop:	Blocks A, B and C
	APIs covered:	• Sitagliptin HCl H2O • Vildagliptin • Pirfenidone • Ticagrelor • Apixaban • Dimethyl Fumarate • Linagliptin • Posaconazole (Form-I) • Macitentan WHO API was not specifically covered
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	The site has never been inspected by the WHO	
Abbreviations	**Meaning**	
BMR	Batch manufacturing record	
BPR	Batch production record	
CAPA	Corrective action and preventive action	
CC	Change control	
GMP	Good manufacturing practices	
HVAC	Heating ventilation and air-conditioning system	
SRA	Stringent regulatory agency	
OOS	Out-of-specifications	
OOT	Out-of-trends	

PQR	Product quality review
SOP	Standard operating procedure
QMS	Quality management system

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

a) Manufacturing authorization and GMP certificate granted by the local authority:
License: 26/VP/AP/2013/B/R , valid up to 29.08.2023
Government of Andhra Pradesh Drugs Control Administration GMP certificate No 12747/DD/DCA/VSP/2019, valid up to 31.10.2020.

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 (intermediates, dosage forms) manufactured on-site:
54 APIs are manufactured at the site:

- Anti – diabetics
- Anti – coagulants
- Norepinephrine reuptake inhibitor
- Erectile Dysfunction agent
- Anti - hypertensive
- Anti - psychotic agent
- Anti - convulsant
- Anti-retroviral
- Anti-Gout
- Atopic dermatitis
- Iodine X-ray contract agents
- Multiple sclerosis
- Anti – diarrheal, gastrointestinal agent
- Anti – dyspareunia agent
- Anti – fibrotic
- Anti – fungal
- Cardiovascular agent
- PAH activator
- Anti – viral
- Reversal of Neuromuscular blockade and reversal of nondepolarizing muscle relaxants
- Anti - platelet

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

Name of inspected authority	Dates of inspection	Outcome
USFDA, USA	11-15 November 2019	EIR received, inspection closed
	19 – 23 June 2017	EIR received, inspection closed
	17-21 August 2015	EIR received, inspection closed
OGYEI, Hungary	20 – 27 November 2019	GMP certificate issued
Ministry of Industry and Trade of Russian Federation, Russia	10 – 13 October 2018	GMP certificate issued
German Authority	5 – 6 July 2016	GMP certificate issued
MFDS, Korea	22 – 25 February 2016	GMP certificate issued
TGA, Australia	26 – 29 April 2016	GMP certificate issued

e) Most recent product quality review (PQR) of the concerned WHO API:
3 Remdesivir validation batches has been manufactured, therefor PQR for Clobazam was reviewed

f) Batch manufacturing and packaging records, including the analytical part, for the most recently released batch of relevant API:
Submitted and reviewed Remdesivir:
- BMR/BPR stage I, stage II, stage III and stage HR (finished API)
- Analytical raw data (intermediate) No XX
- Analytical raw data (intermediate) No YY
- Analytical raw data (finished API) No ZZ

g) Master batch manufacturing and packaging records of the API of interest:
Submitted and reviewed Remdesivir:
- Master batch record – drying, micro-pulverization, sifting and packaging
- Master batch record – stage I
- Master batch record – stage II
- Master batch record – stage III (finished API)

h) Recalls in the past three years related to APIs with quality defects:
Declaration submitted: no recalls in the past 3 years

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: a full self-inspection or external audit dedicated to the API has been performed and all matters dealt with

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 or equivalent regulatory action, issued

k) Out-of-stock situations:
Declaration submitted: no out-of-stock situations

l) Additional documents submitted:
"SOP "Preparation of Annual product quality review"

Part 5	**Conclusion – Desk assessment outcome**

Based 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 ***Honour Lab Limited, Unit III (Block A, manufacturing section VII),*** located at ***Plot 4, Hetero Infrastructure Ltd., SEZ, N. Narasapuram Village, Nakkapally, Visakhapatnam, Andhra Pradesh, 531081, 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.

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

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 2.
   Short name: WHO TRS No. 957, Annex 2
   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