

**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	GVK Biosciences Pvt. Ltd.	
Corporate address of manufacturer	GVK Biosciences Pvt Ltd Plot 28-A IDA, Nacharam, Medchal-Malkajgiri District Telangana, Hyderabad, 500 076, India Telephone Number(s): +91 40 6692 9999, Fax: +91 40 6692 9900	
Inspected site		
Name & address of manufacturing site	GVK Biosciences Pvt. Ltd. Plot 28-A IDA, Nacharam, Medchal-Malkajgiri District Telangana, Hyderabad, 500 076, India GPS details: Latitude: 17.4360955° Longitude: 78.5597527° Telephone Number(s): +91 40 6692 9999 Fax: +91 40 6692 9900	
Synthetic Unit/Block/Workshop	Moxifloxacin hydrochloride is manufactured at GVK Biosciences Private Limited, Unit-1, Block-A.	
Desk assessment details		
Date of review	28 August 2019 to 15 November 2019	
APIs covered by this desk assessment	Moxifloxacin HCL (APIMF205)	
Part 2	Summary of SRA/NRA inspection evidence considered (from most recent to last) and comments	
US FDA	Dates of inspection:	30.04.18 to 04.05.18 (5 days)
	Type of inspection:	Routine (the site mentioned in the FDA report is Inogent (subsidiary of GVK))
	Block/Unit/Workshop:	Block A and B
	APIs covered:	APIs by chemical synthesis
Abbreviations	Meaning	
BMR	Batch manufacturing record	
BPR	Batch production record	
CAPA	Corrective and preventive action	
CoA	Certificate of analysis	
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 3	Summary of the assessment of supporting documentation
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a) Manufacturing authorization and GMP certificate granted by the local authority:

License number 120/HD/AP/97/B/R renewed on the 28/11/1997 by the Drug control administration of Telangana and is valid until 27-05-2023.

b) Site master file (SMF): Site master file, document number M, PIC\S, WHO-TRS 823 effective date 25.01.2019

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

A list of all products manufactured at the site was presented, there were no beta lactam or cytotoxic products manufactured at the site. There is no concern with regards to cross-contamination. Previous reports indicated that systems and procedures such as cleaning validation, cleaning methods, air filtration and pressure cascades which should cater for any risks of product cross-contamination during manufacture were available and adequate.

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

The following SRA inspections were conducted:

-USFDA from 10.08.2015 to 13.08.15 on Inogent laboratories, the facility was rated compliant. An EIR was issued. All these were closed with a compliant rating, but this inspection was older than 3 years

-EDQM on 22-02-2018 (desk assessment)

-USFDA from 30-april-2018 to 04-May-2018 for Inogent laboratories, with a focus on Tramadol hydrochloride.

-PMDA from 22-may-2018 to 25-May-2018, focussing on Tramadol hydrochloride.

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

APQRs for the PQ product was submitted. PQR for Moxifloxacin HCL, reviewed from Jan 20018 to Dec 2018.

The APQR reports included a review of starting and product critical quality attributes, critical process and In-process control, review of out of trends and OSS investigation, deviations, market complaints, product recalls, deviations, CAPA, change controls, returned goods, stability data, qualification status of relevant equipment, utility, systems, facility and process validation, cleaning validation.

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

The BMR for Moxifloxacin HCL, batch number MF100319, manufacture date 10/01/19, batch size 150 Kg was sampled for review. The records were generally well assembled and detailed, and included line clearance before each critical stage, raw material testing and approval records, raw material dispensing records, instructions for each processing stage with time duration where required, sampling for in-process controls and records of in-process test results. The finished product CoA was verified against WHO listed product specifications and batch release records. The BMR reviewed was found acceptable.

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

Blank master batch manufacturing and packaging records of the above listed PQ product were submitted.

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

Recall statements from head of quality assurance confirming that no recalls were executed in the past three years for products manufactured at GVK site.

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:

A statement by the head of Quality Assurance mentioning was provided alongside a list of external regulatory audits performed for PQ products. CAPAs, where applicable, were attached.

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 regulatory inspection statement by the head of Quality Assurance, mentioning that no notice of concern, warning letter or equivalent regulatory actions were issued to GVK by any Authority.

k) Out-of-stock situations: There were no out-of-stock situations in the last 3 years.

l) Additional documents submitted: None

Part 4	Conclusion – Desk assessment outcome
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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 ***GVK Biosciences Pvt Ltd*** located at ***Plot 28-A IDA, Nacharam, Medchal-Malkajgiri District, Telangana, Hyderabad, 500 076, India*** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines.

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.

Part 5	List of guidelines referenced in this inspection report
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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. 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/
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