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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	Chromo Laboratories India Private Limited
Corporate address of manufacturer	Plot No. 43 & 44, Phase II, I.D.A, Pashamylaram, Patancheru Mandal, Sangareddy District-502 307, Telangana State, India Tel.: +91 9490757602, Fax: +91 8455 297020 E mail: info@chromolabs.com 24-hour telephone numbers: +91 9490757602
Inspected site	
Name & address of manufacturing site	Chromo Laboratories India Private Limited, Plot No. 43 & 44, Phase II, I.D.A, Pashamylaram, Patancheru Mandal, Sangareddy District-502 307, Telangana State, India GPS details: Latitude:17º32´20.90"N Longitude:78º10´56.80"E(Gate) D-U-N-S Number:91 5368300 Tel.: +91 9490 757602 Fax: +91 8455 297020
Synthetic Unit/Block/ Workshop	Block-A & Block-C (Module-1)
Desk assessment details	
Date of review	17 September 2019
APIs covered by this desk assessment	Moxifloxacin Hydrochloride
List of documents submitted	• List of regulatory inspections performed at the site during the last 5 years. • EDQM inspection report, proof of CAPA implementation and final decision by the EDQM. • GMP Confirmation letter written by Central Drugs Standard Control Organization, India. • Manufacturing license, number 16/MD/AP/2008/B/R issued on the 12/06/2018 by the Drugs Control Administration (Telangana State) valid till 15/06/2023. • GMP Certificate, number 8627/E1/2018 issued on the 28/01/2019 by the Drugs Control Administration (Telangana State) valid for one year • Site master file, effective date 24.08.2019

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	• list of all the products manufactured on-site • The APQR report for Moxifloxacin Hydrochloride. • Completed BMRs for Moxifloxacin Hydrochloride. • Blank BMR for Moxifloxacin Hydrochloride. • Recall statement: that no recalls were executed in the past three years. • Self-inspections statement: self-inspections were performed for Moxifloxacin Hydrochloride and all matters are dealt with. • A regulatory inspection statement by the Dy. Manager-Quality Assurance, mentioning that no notice of concern, warning letter or equivalent regulatory actions were issued to Chromo Laboratories India Private Limited by any Authority. • A statement by the Dy. Manager-Quality Assurance, confirming that out of stock situation is not applicable.	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last)**	
EDQM	Dates of inspection:	5-7/2/2018
	Type of inspection:	Pre-approval inspection
	Block/Unit/Workshop:	Block-A and Block-C
	Type of APIs covered:	API by chemical synthesis
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	*None*	
Brief description of manufacturing activities	According to the SMF, the site is involved in manufacturing of advanced intermediates and API only. Cephalosporins, Hormones and cytotoxic drugs are not manufactured at the site.	
General information about the company and manufacturing site	According to the SMF, the site is advanced intermediates and API facility comprises of manufacturing facility and process development lab, Quality control department, Quality Assurance department, Safety, Health and environment department, Ware house facilities and Human resources department.	
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	

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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:

- Manufacturing license, No. 16/MD/AP/2008/B/R
- Issued:12/06/2018 by the Drugs Control Administration (Telangana State)
- Valid: 15/06/2023
- Levofloxacin Hemihydrate-USP&IP, Moxifloxacin HCl-BP/USP/Ph.Eur were approved according to the License.

- GMP Certificate, No. 8627/E1/2018
- Issued:28/01/2019 by the Drugs Control Administration (Telangana State)
- Valid: one year

b) Site master file (SMF):

Site master file, effective date 24.08.2019, with annexures of legible color printouts of water treatment and air handling systems, including pipeline and instrumentation drawings was reviewed and found acceptable and in line with the WHO TRS No. 961, Annex 14.

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

1.Atazanavir sulfate
2.Atorvastatin Calcium(ATR)
3.Candesartan Cilexetil
4.Chlorthalidone
5.Dolutegrvir
6.Levocitrizine hydrochloride
7.Levofloxacin Hemihydrate
8.Moxifloxacin hydrochloride
9.Olanzapine
10.Olmesartan Medoxomil
11.Repaglinide
12.Telmisartan
13.Terbinafine Hydrochloride
14.Valsartan
15.Vadfenafil Hydrochloride

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16.Voriconazole
17.Zafirlukast
18.Zafirlukast Premix
19.Ziprasidone

There were no beta-lactam or cytotoxic products manufactured at the site.

d) List of all regulatory inspections performed in the last 3 years and their outcomes:
The only SRA inspection conducted at the site within the last 3 years was by EDQM from the 5.2.2018 to 7.2.2018. EDQM-GMP compliant.

e) Most recent product quality review(s) (PQR)(s) of the concerned WHO API(s):
Annual Product Quality Review of Moxifloxacin Hydrochloride shows that there are two stages for Moxifloxacin Hydrochloride production. The PQR reviewed the intermediates, key starting material, primary packaging material, in-process quality control tests, critical process parameters, intermediate quality and finished product quality. All batches trend data found well within the acceptance limits.

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

- Moxifloxacin Hydrochloride Stage-1 (MNC-1) executed Batch production record (Batch No.XXX), manufacture date 18/04/2019.
- Moxifloxacin Hydrochloride Stage-1 (MNC-1) executed analytical record (Batch No. XXX), report date 30/04/2019.
- Moxifloxacin Hydrochloride Stage-2 (MNC-2) executed Batch production record (Batch No. XXX), manufacture date 08/06/2019.
- Moxifloxacin Hydrochloride Stage-2 (MNC-2) executed analytical record (Batch No.XXX).
- Moxifloxacin Hydrochloride Packing record (Batch No. XXX), manufacture date 07/2019.
- Moxifloxacin Hydrochloride Certificate of analysis (COA, Batch No. XXX)

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 products were submitted.

h) Recalls in the past three years related to APIs with quality defects:
Recall statements from the Dy. Manager-Quality Assurance stating that no recalls were executed in the past three years for products manufactured at Chromo Laboratories India Private Limited.

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 Dy. Manager-Quality Assurance mentioning that self-inspections were performed for Moxifloxacin Hydrochloride and all matters are dealt with.

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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 Dy. Manager-Quality Assurance, mentioning that no notice of concern, warning letter or equivalent regulatory actions were issued to Chromo Laboratories India Private Limited by any Authority.

k) Out-of-stock situations:

A statement by the Dy. Manager-Quality Assurance, confirming that out of stock situation is not applicable.

l) Additional documents submitted:

None.

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 **Chromo Laboratories India Private Limited** located at ***Plot No. 43 & 44, Phase II, I.D.A, Pashamylaram, Patancheru Mandal, Sangareddy District, Telangana, 502 307, India*** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines for APIs.

This WHOPIR will remain valid until 7 February 2021 (3 years from the last EDQM GMP inspection), 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 ***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*. Forty-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

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