## Part 1
### General information

#### Company information

<table>
<thead>
<tr>
<th>Name of Manufacturer</th>
<th>Cipla Limited</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corporate address of manufacturer</td>
<td>Cipla House Peninsula Business Park Ganpatrao Kadam Marg Lower Parel, Mumbai 400013 India</td>
</tr>
</tbody>
</table>

#### Inspected site

<table>
<thead>
<tr>
<th>Name &amp; address of manufacturing site</th>
<th>Cipla limited Old Madras Rd Virgonagar District Bengaluru Karnataka, 560 049 India</th>
</tr>
</thead>
<tbody>
<tr>
<td>DUNS:</td>
<td>915154892</td>
</tr>
<tr>
<td>Synthetic Unit/Block/Workshop</td>
<td>Synthetics I, Synthetics VII, API Finishing Area</td>
</tr>
</tbody>
</table>

#### Desk assessment details

| Date of review | 19 July 2022 |
| APIs covered by this desk assessment | Not specific – general review of GMP compliance as per EU inspection information including Zidovudine, Granisetron, Amlodipine besilate |

## Part 2
### Summary of SRA/NRA inspection evidence considered (from most recent to last) and comments

#### Finnish Medicine Agency, on behalf of EMA

| Dates of inspection: | 27 to 31 January 2020 |
| Type of inspection: | General GMP |
| Block/Unit/Workshop: | API Block III and V, Lab Production II and Finishing area |
| APIs covered: | Amlodipine Granisetron Zidovudine |

#### US FDA, USA

| Dates of inspection: | 15 to 19 July 2019 |
| Type of inspection: | cGMP |
| Block/Unit/Workshop: | Included API Block III / IV |
| APIs covered: | Synthetic small molecule |
### Part 3  
**Summary of the last WHO inspection**

| Date and conclusion of most recent WHO inspection | Cipla Bangalore was considered to be operating at an acceptable level of compliance with WHO GMP guidelines: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients. The inspection was closed out on 20th April 2014.  
A desk review was also done in 2020. |
| Brief summary of manufacturing activities | Production operations in buildings API-I, API-III and Synthetics-VII were covered. Production and packaging of Vinblastin Sulphate took place in block API-I. Levofloxacin Hemihydrate and Ritonavir were manufactured in block API-III and finishing and packaging steps were carried out in block Synthetics VII. |
| General information about the company and manufacturing site | Cipla was established in 1935 and it is managed by a board of directors. It manufactures and distributes a wide range of FPPs and APIs which are registered in several countries around the world. The headquarters are located at Mumbai and there are several manufacturing and R&D sites established in India.  
The site in Virgonagar was first licensed in 1978 and it is authorized to manufacture APIs for FPPs intended for human use. The manufacturing facilities are located approximately 45Km from Bangalore airport. The campus consists of separate blocks for the manufacture of APIs and intermediates. Anticancer APIs are manufactured in dedicated areas. According to the company antineoplastics are handled with sufficient operational controls and change over procedures. Finishing areas are located in separate blocks: Synthetics-I, Synthetics-VII, API Block-III, API Block-IV, Lab production and API Block-V. All APIs are manufactured in campaigns. |
| Focus of the last WHO inspection | The 2014 WHO PQ inspection covered the production and control of Levofloxacin, Ritonavir and Vinblastine. The inspection reviewed most of the sections of WHO GMP for APIs, including Quality Management; Personnel; Buildings and Facilities; Process Equipment; Documentation and Records; Materials Management; Production and In-Process Controls; Packaging and Identification Labelling of APIs and Intermediates; Storage and Distribution; Laboratory Controls; Validation; Change Control; Rejection and Reuse of Materials and Complaints and Recalls  
A desk review was done in 2020. |
| Areas inspected | The 2014 WHO PQ inspection focused on manufacturing, quality control and packaging activities of:  
APIMF156 Vinblastin Sulphate (production and packaging in workshop API-I)  
APIMF088 Levofloxacin Hemihydrate (production excluding finishing in workshop API-III and finishing and packaging in workshop Synthetics VII)  
APIMF 215 Ritonavir (production excluding finishing in workshop API-III and finishing and packaging workshop Synthetics VII) |
Out of scope and restrictions (last WHO inspection) | N/A

WHO APIs covered by the last WHO inspection:
- APIMF 156 Vinblastine Sulphate (production and packaging in workshop API-I)
- APIMF 088 Levofloxacin Hemihydrate (production excluding finishing in workshop API-III and finishing and packaging in workshop Sysnthetics VII)
- APIMF 215 Ritonavir (production excluding finishing in workshop API-III and finishing and packaging workshop Sysnthetics VII)

Additional products to be covered by this desk assessment:

<table>
<thead>
<tr>
<th>PQT Number</th>
<th>API</th>
<th>Prequalification status</th>
</tr>
</thead>
<tbody>
<tr>
<td>APIMF088</td>
<td>Levofloxacin hemihydrate</td>
<td>Accepted</td>
</tr>
<tr>
<td>APIMF004b</td>
<td>Artesunate</td>
<td>Accepted</td>
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</table>

Note: Artesunate is no longer manufactured

### Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Meaning</th>
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<tbody>
<tr>
<td>BMR</td>
<td>Batch manufacturing record</td>
</tr>
<tr>
<td>BPR</td>
<td>Batch production record</td>
</tr>
<tr>
<td>CAPA</td>
<td>Corrective and preventive action</td>
</tr>
<tr>
<td>CC</td>
<td>Change control</td>
</tr>
<tr>
<td>GMP</td>
<td>Good manufacturing practices</td>
</tr>
<tr>
<td>NC</td>
<td>Non conformity</td>
</tr>
<tr>
<td>NRA</td>
<td>National regulatory agency</td>
</tr>
<tr>
<td>PQR</td>
<td>Product quality review</td>
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<tr>
<td>PQS</td>
<td>Pharmaceutical quality system</td>
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<tr>
<td>QA</td>
<td>Quality assurance</td>
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<tr>
<td>QC</td>
<td>Quality control</td>
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<tr>
<td>QCL</td>
<td>Quality control laboratory</td>
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<tr>
<td>QMS</td>
<td>Quality management system</td>
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<tr>
<td>QRM</td>
<td>Quality risk management</td>
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<tr>
<td>RA</td>
<td>Risk assessment</td>
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<tr>
<td>RCA</td>
<td>Root cause analysis</td>
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<tr>
<td>SOP</td>
<td>Standard operating procedure</td>
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### Part 4

#### Summary of the assessment of supporting documentation

**a) Manufacturing authorization and GMP certificate granted by the local authority:**
The manufacturing license and GMP compliance documentation were submitted. Valid until 31/12/2026.

**b) Site master file (SMF):**
A detailed SMF dated 12 July 2022 was submitted and found acceptable.
c) List of all the APIs or other products (intermediates, dosage forms) manufactured on-site: Reviewed. No issues of concern were found.

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

![List of Regulatory Inspections](image)

Ten (10) batches were produced and included in the PQR. There were no reprocessed batches, no returns, recalls or complaints. There was one OOS result reported and investigated. Results were trended and PpK calculated. Generally, the PQR was acceptable.

Artesunate batches FWA190004, FWA190005, FWA190006 were micronized in the period of 2019 and thereafter no other batches have been manufactured.

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

APQR (Annual product quality review) of Levofloxacin hemihydrate attached was submitted.

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

Levofloxacin - Batch: FDC 210447 production and analytical record submitted, manufactured in September 2021
Levofloxacin USP - Batch FDP210263 submitted, manufactured November 2021
LVF 4, Batch Manufacturing Record: Batch FDC210555 Analytical report

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

Levofloxacin Hemihydrate MBMR and MBPR submitted.
LVF-4 (Intermediate of Levofloxacin) MBMR submitted.
Generally, the BMR was acceptable.
Artesunate: Obsolete since 2019.
h) Recalls in the past three years related to APIs with quality defects:
There was no recall in the past three years related to any product manufactured on site with quality defects.

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 letter was submitted stating that self-inspections are conducted and CAPAs are implemented.

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):
Not applicable

k) Out-of-stock situations:
No out-of-stock situation is foreseen

l) Additional documents submitted:
None

m) The following information regarding waste management practices (As per WHO points to consider for manufactures and inspectors: environmental aspects of manufacturing for the prevention of antimicrobial resistance”, Technical report series 1025, Annex 6):

Disposal procedure of Levofloxacin Hemihydrate product waste (Liquid and solid) - All waste generated at site are evaluated by External agency M/S ERM (Environmental Resource Management). The collected waste from Levofloxacin Hemihydrate are segregated separately and sent to authorized 3rd party E-NANO, Bangalore for thermal destruction through regulatory requirements as per Hazardous waste rule 2016. After the destruction, destruction certificate from vendor are received to ensure incineration.

Disposal of the liquid and solid waste, that contain residues of Levofloxacin Hemihydrate API and of its intermediates, generated during the Levofloxacin Hemihydrate manufacturing process: For the disposal of Levofloxacin Hemihydrate API and of its intermediates, generated during the Levofloxacin Hemihydrate manufacturing process following procedure is followed. All the liquid and solid waste from levofloxacin hemihydrate product are collected separately. Collected waste liquid and solid are sent to KSPCB (Karnataka State pollution Control Board) authorized incinerator with manifest Form 10. Post completion of incineration, certificate is received as evidence. This process is carried out by an external agency M/S ERM. Decontamination methods are not used for waste management of liquid waste as the liquid waste is not released to sewers/streams or into the municipality water.

Note: In general, these were found acceptable. Due to time constraints, documents were briefly reviewed and an in-depth inspection was not done.
**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 Cipla Ltd, located at Old Madras Rd, Virgonagar, District - Bengaluru, Karnataka, 560 049, India is considered to be operating at an acceptable level of compliance with WHO GMP guidelines for APIs.

This WHOPIIR 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**

   [untitled (digicollections.net)]

   [https://digicollections.net/medicinedocs/documents/s21467en/s21467en.pdf]

   [https://digicollections.net/medicinedocs/documents/s23457en/s23457en.pdf]

   [9789240020900-eng.pdf (who.int)]

   [https://digicollections.net/medicinedocs/documents/s21440en/s21440en.pdf]


https://digicollections.net/medicinedocs/#d/s21438en


https://digicollections.net/medicinedocs/#d/s20177en/

https://digicollections.net/medicinedocs/#d/s20175en/

http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1


Essential Medicines and Health Products Information Portal (digicollections.net)


9789240020900-eng.pdf (who.int)


Short name: WHO TRS No. 992, Annex 6


9789240020900-eng.pdf (who.int)