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

<table>
<thead>
<tr>
<th>Part 1</th>
<th>General information</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Company information</strong></td>
<td></td>
</tr>
<tr>
<td>Name of Manufacturer</td>
<td>Mylan Laboratories Limited (Unit-10)</td>
</tr>
</tbody>
</table>
| Corporate address of manufacturer | M/s. Mylan Laboratories Limited  
Plot No 564/A/22,  
Road No 92,  
Jubilee Hills,  
Hyderabad-500096  
Telangana, India |
| **Inspected site** | |
| Name & address of manufacturing site | Mylan Laboratories Limited (Unit-10), Plot No. 86, Ramky Pharma City (India) Ltd, JN Pharma City, Parawada Mandal, Visakhapatnam, Andhra Pradesh, 531019, India |
| Synthetic Unit/Block/Workshop | • MB-4 BAY-2 Pharma area (API)  
• MB-4 BAY-2 Intermediate area  
• MB-3 Intermediate area  
• MB-2 Intermediate area  
• MB-4 BAY-1 Pharma area  
• MB-4 BAY-3 Pharma area  
• MB-1 Intermediate area  
• MB-3 BAY-1 & BAY – 2 Pharma areas |
| **Desk assessment details** | |
| APIs covered by this desk assessment | • Abacavir hemisulfate  
• Tenofovir disoproxil fumarate  
• Efavirenz |
| List of documents submitted | 1. ANVISA Certificate  
2. MFDS audit response and certificate  
3. USFDA EIR  
4. Manufacturing License copy of Abacavir Sulfate, Efavirenz and Tenofovir Disoproxil Fumarate  
5. GMP certificate copy of Abacavir Sulfate, Efavirenz and Tenofovir Disoproxil Fumarate  
6. Site Master File & Annexures  
7. List of APIs with proprietary names and INN  
8. PQRs for:  
   a. Abacavir Sulfate APQR Summary report  
   b. Abacavir Sulfate APQR Annexures  
   c. Efavirenz APQR Summary report  
   d. Efavirenz APQR Annexures  
   e. Tenofovir Disoproxil Fumarate APQR Summary report  
   f. Tenofovir Disoproxil Fumarate APQR Annexures  
   g. Annual review of Manufacturing Supporting Systems |
h. Annual review of packaging materials

9. Completed Manufacturing Batch Production Records and Analytical Data for:
   a) Abacavir sulfate:
      1. Executed MBPR
      2. In-process Results
      3. Analytical data
   b) Efavirenz:
      1. Executed MBPR
      2. In-process Results
      3. Analytical data
   c) Tenofovir Disoproxil Fumarate:
      1. Executed MBPR
      2. In-process results
      3. Analytical data

11. Abacavir Sulfate Master Batch Production Record
12. Efavirenz Master Batch Production Record
13. Tenofovir Disoproxil Fumarate Master Batch Production Record
14. Declaration for Recalls
15. Declaration for self-inspection
16. Declaration for Warning letters
17. Declaration for Out of stock

Part 2

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

<table>
<thead>
<tr>
<th>US FDA</th>
<th>Dates of inspection:</th>
<th>29.10.2018 to 02.11.2018</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Type of inspection:</td>
<td>Routine inspection</td>
</tr>
<tr>
<td></td>
<td>Block/Unit/Workshop:</td>
<td>MB1; MB2; MB3; MB4; and MB4 Bays 2 and 3</td>
</tr>
<tr>
<td></td>
<td>APIs covered:</td>
<td>• Tenofovir Disoproxil Fumarate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Abacavir Sulfate USP</td>
</tr>
</tbody>
</table>

Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Meaning</th>
</tr>
</thead>
<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>
</tr>
<tr>
<td>POS</td>
<td>Pharmaceutical quality system</td>
</tr>
<tr>
<td>QA</td>
<td>Quality assurance</td>
</tr>
<tr>
<td>QC</td>
<td>Quality control</td>
</tr>
<tr>
<td>QCL</td>
<td>Quality control laboratory</td>
</tr>
<tr>
<td>QMS</td>
<td>Quality management system</td>
</tr>
<tr>
<td>QRM</td>
<td>Quality risk management</td>
</tr>
<tr>
<td>RA</td>
<td>Risk assessment</td>
</tr>
<tr>
<td>RCA</td>
<td>Root cause analysis</td>
</tr>
<tr>
<td>SOP</td>
<td>Standard operating procedure</td>
</tr>
</tbody>
</table>
**Part 3  Summary of the assessment of supporting documentation**

**a) Manufacturing authorization and GMP certificate granted by the local authority:**
Form 26 No 34/VP/AP/2012/8/R, granted on the 22-08-2012 has been renewed from 22-08-2017 to 21-08-2022.

**b) Site master file (SMF):**
Submitted – acceptable, prepared according to the WHO TRS No. 961, Annex 14

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

<table>
<thead>
<tr>
<th>No.</th>
<th>Product Name</th>
<th>Proprietary Name</th>
<th>INN</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tenofovir Disoproxil Fumarate</td>
<td>VIREAD</td>
<td>Tenofovir Disoproxil Fumarate</td>
</tr>
<tr>
<td>2</td>
<td>Citalopram Hydrobromide</td>
<td>CELEXA</td>
<td>Citalopram Hydrobromide</td>
</tr>
<tr>
<td>3</td>
<td>Efavirenz</td>
<td>SUSTIVA</td>
<td>Efavirenz</td>
</tr>
<tr>
<td>4</td>
<td>Tenofovir Disoproxil Maleate</td>
<td>--</td>
<td>Tenofovir Disoproxil Maleate</td>
</tr>
<tr>
<td>5</td>
<td>Abacavir Sulfate</td>
<td>ZIAGEN</td>
<td>Abacavir Sulfate</td>
</tr>
<tr>
<td>6</td>
<td>Elvitegravir</td>
<td>VITEKTA</td>
<td>Elvitegravir</td>
</tr>
<tr>
<td>7</td>
<td>Tenofovir Alafenamide Fumarate</td>
<td>VEMLIDY</td>
<td>Tenofovir Alafenamide Fumarate</td>
</tr>
<tr>
<td>8</td>
<td>Tenofovir Disoproxil Orotate</td>
<td>--</td>
<td>Tenofovir Disoproxil Orotate</td>
</tr>
<tr>
<td>9</td>
<td>Carvedilol</td>
<td>COREG</td>
<td>Carvedilol</td>
</tr>
<tr>
<td>10</td>
<td>Carvedilol Phosphate</td>
<td>COREG CR</td>
<td>Carvedilol Phosphate</td>
</tr>
<tr>
<td>11</td>
<td>Escitalopram Oxalate</td>
<td>LEXAPRO</td>
<td>Escitalopram Oxalate</td>
</tr>
<tr>
<td>12</td>
<td>Mafenide Acetate</td>
<td>SULFAMYLON</td>
<td>Mafenide Acetate</td>
</tr>
<tr>
<td>13</td>
<td>Esomeprazole Magnesium Trihydrate</td>
<td>NEXIUM</td>
<td>Esomeprazole Magnesium Trihydrate</td>
</tr>
<tr>
<td>14</td>
<td>Sucroferric oxyhydroxide</td>
<td>VELPHORO</td>
<td>Sucroferric oxyhydroxide</td>
</tr>
<tr>
<td>15</td>
<td>Dolutegravir Sodium</td>
<td>TIVICAY</td>
<td>Dolutegravir Sodium</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Date of Inspection</th>
<th>Name of the Regulatory Agency</th>
<th>Name of the Country</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>07.09.2015 to 11.09.2015</td>
<td>USFDA</td>
<td>USA</td>
<td>Approved</td>
</tr>
<tr>
<td>30.09.2015</td>
<td>WHO (Desk Review)</td>
<td>Geneva</td>
<td>Approved</td>
</tr>
<tr>
<td>16.12.2015 to 17.12.2015</td>
<td>AGES</td>
<td>Austria</td>
<td>Approved</td>
</tr>
<tr>
<td>24.10.2016 to 26.10.2016</td>
<td>MFDS</td>
<td>Korea</td>
<td>Approved</td>
</tr>
<tr>
<td>18.05.2017 to 19.05.2017</td>
<td>CDSCO &amp; DCA</td>
<td>India</td>
<td>Approved</td>
</tr>
</tbody>
</table>
e) Most recent product quality reviews (PQRs) of the concerned WHO APIs:
Submitted and reviewed for:
1) Abacavir Sulfate APQR
   a) Summary report
   b) Annexures
2) Efavirenz APQR
   a) Summary report
   b) Annexures
3) Tenofovir Disoproxil Fumarate
   a) APQR Summary report
   b) Annexures
4) Annual review of Manufacturing Supporting Systems
5) Annual review of packaging materials

f) Batch manufacturing and packaging records, including the analytical part, for the most recently released batch of relevant APIs:
Submitted and reviewed for:
1) Abacavir Sulfate:
   a) Executed MBPR
   b) In-process Results
   c) Analytical data
2) Efavirenz:
   a) Executed MBPR
   b) In-process Results
   c) Analytical data
3) Tenofovir Disoproxil Fumarate:
   a) Executed MBPR
   b) In-process results
   c) Analytical data

g) Master batch manufacturing and packaging records of the APIs of interest:
Submitted and reviewed for:
1) Abacavir Sulfate Master Batch Production Record
2) Efavirenz Master Batch Production Record
3) Tenofovir Disoproxil Fumarate Master Batch Production Record

h) Recalls in the past three years related to APIs with quality defects:
Submitted: Declared - no recalls

i) Confirmation by the senior quality assurance representative that a full self-inspection or external audit dedicated to the APIs has been performed and all matters dealt with:
Submitted
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):
Submitted: Declared - no warning letters

k) Out-of-stock situations:
Submitted: Declared - no out-of-stock

l) Additional documents submitted:
N/A

Part 4  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 Mylan Laboratories Limited (Unit-10) located at Plot No. 86, Ramky Pharma City (India) Ltd, JN Pharma City, Parawada Mandal, Visakhapatnam, Andhra Pradesh, 531019, 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 5  List of guidelines referenced in this inspection report


   https://www.who.int/medicines/areas/quality_safety/quality_assurance/TRS1010annex9.pdf?ua=1

   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/


Short name: WHO TRS No. 961, Annex 9
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

http://whqlibdoc.who.int/trs/WHO_TRS_943_eng.pdf?ua=1


Short name: WHO TRS No. 961, Annex 2
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1


Short name: WHO TRS No. 981, Annex 2
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/


Short name: WHO TRS No. 981, Annex 3
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/


Short name: WHO TRS No. 961, Annex 14
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1


Short name: WHO TRS No. 992, Annex 3


Short name: WHO TRS No. 992, Annex 4

http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf
