Prequalification Team Inspection services  
WHO PUBLIC INSPECTION REPORT  
(WHOPIR)  

Desk Assessment of Finished Pharmaceutical Product (FPP) Manufacturer

<table>
<thead>
<tr>
<th>Part 1</th>
<th>General information</th>
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<tbody>
<tr>
<td><strong>Company information</strong></td>
<td></td>
</tr>
<tr>
<td>Name of Manufacturer</td>
<td>Mylan Laboratories Limited</td>
</tr>
</tbody>
</table>
| Corporate address of manufacturer | Mylan Laboratories Limited  
Plot No. 564/A/22, Road No. 92, Jubilee Hills, Hyderabad - 500 034, Telangana, India  
Telephone Number: +91-40-30866666, 23550543  
Fax Number: +91-40-30866699  
Site: www.mylanlabs.in |
| Inspected site | |
| Name & address of manufacturing site | Mylan Laboratories Limited, Ahmedabad  
Sarkhej- Bavla NH No- 8A, Plot No 20/21 Pharmaceutical Special Economic Zone, Nr Village Matoda, Ahmedabad, Gujarat, 382213, India  
D-U-N-S 677604150, latitude 22.874 N, longitude 72.402 E |
| Production Block/Unit | Injectables (by terminal autoclave sterilization) and OSDs (Oral Solid Dosage forms) |
| Desk assessment details | |
| Date of review | 5 March 2019 |
| Products covered by this desk assessment | Oral and injectable contraceptives. Specific products assessed:  
1. Levonorgestrel Tablet 1.5mg  
2. Levonorgestrel Tablet 750 mcg  
3. Desogestrel/Ethinylestradiol Tablet 0.150mg/0.030mg  
4. Ethinylestradiol/Levonorgestrel + Ferrous Fumarate Ethinylestradiol/Levonorgestrel Tablet + Placebo (Ferrous Fumarate Tablet) 30mcg/150mcg + 75mg  
5. Desogestrel/Ethinylestradiol + Placebo Desogestrel/Ethinylestradiol Tablet + Placebo Tablet 150mcg/30mcg + 0mcg  
6. Levonorgestrel Tablet, Film-coated 0.03mg  
7. Medroxyprogesterone acetate Suspension for injection 150mg/ml |

<table>
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<tr>
<th>Part 2</th>
<th>Summary of SRA/NRA inspection evidence considered (from most recent to last)</th>
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<tbody>
<tr>
<td>US FDA</td>
<td>Dates of inspection: 23-29 August 2017</td>
</tr>
<tr>
<td>Type of inspection:</td>
<td>Pre-approval inspection</td>
</tr>
<tr>
<td>Block/Unit:</td>
<td>Main production block section for injectable products</td>
</tr>
<tr>
<td>Type of products/Dosage forms covered:</td>
<td>Small volume parenterals</td>
</tr>
<tr>
<td>US FDA</td>
<td>Dates of inspection: 20-24 November 2017</td>
</tr>
<tr>
<td>Part 3</td>
<td>Summary of the last WHO inspection</td>
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<tr>
<td><strong>Date and conclusion of most recent WHO inspection</strong></td>
<td>18-21 April 2016 for the manufacturing of OSDs only. Compliant 3-6 September 2012 for the manufacturing of OSDs only. Compliant</td>
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<tr>
<td><strong>Brief description of manufacturing activities</strong></td>
<td>Coated and Uncoated Tablets with focus on reproductive health products (Oral Contraceptives and support placebos).</td>
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<tr>
<td><strong>General information about the company and manufacturing site</strong></td>
<td>According to the SMF, Mylan Laboratories Limited is the Indian Subsidiary of Mylan Inc., USA, which is World's 3rd largest generics and specialty Pharma Company. Mylan Inc., USA was founded in 1961 and has Corporate Headquarters at Pittsburgh, Pennsylvania, United States. Mylan Inc., USA has primary businesses in following areas -  • Generic Pharmaceuticals and Branded Generic Formulations  • Specialty and Brand Pharmaceuticals  • Active Pharmaceutical Ingredients  Mylan Inc. is one of the world's leading quality generic and highest quality product portfolios, product pipeline and a global commercial footprint through operations in North America, EMEA and APAC. Mylan Laboratories Limited, Ahmedabad is engaged in manufacturing of medicinal products solid orals [Hormonal and Non-Hormonal Tablets] and Injectable formulations (Terminally sterilized suspensions). The facility was commissioned in 2009 as part of Famy Care Ltd. In the month of May 2015, Famy Care has demerged its female contraceptive business into &quot;Jai Pharma Limited&quot;. Mylan acquired the Famy Care's female contraceptive business in November 2015. On 20th November 2015, Jai Pharma Limited became part of &quot;Mylan Laboratories Limited&quot;. Presently, Mylan Laboratories Limited, Ahmedabad is supplying medicines to the Government of India, for its National Family Welfare program and is exporting its products to countries in North America, South America, Europe, Africa, Asia and Australia. The Ahmedabad site is accessible by road, railway &amp; Air and is about 450 km towards north of Mumbai, on Ahmedabad-Rajkot highway and is approximately 42 km far from the Ahmedabad airport. The site is located in Pharmez, (The Pharmaceutical Special Economic Zone) with surrounding units engaged in manufacturing of only Pharmaceuticals Formulations Units. Access to the plot is through a security gate, which is manned 24 hours by trained security personnel. The plant is designed to manufacture hormonal tablets, nonhormonal tablets and small volume parenteral.</td>
</tr>
<tr>
<td><strong>Focus of the last WHO inspection</strong></td>
<td>OSDs (with a focus on reproductive health products)</td>
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Areas inspected

The inspection focused on the production and control of finished pharmaceutical products as listed under Part 1. The inspection covered most of the sections of the WHO GMP text, including premises, equipment, documentation, materials, validation, sanitation and hygiene, production, quality control and utilities.

Out of scope and restrictions (last WHO inspection)

Products that are not under PQ, including injectables

WHO products covered by the last WHO inspection

Coated and Uncoated Tablets:
1. RH031 Levonorgestrel Tablet 1.5mg
2. RH032 Levonorgestrel Tablet 750mcg
3. RH037 Desogestrel/Ethinylestradiol Tablet 0.150mg/0.030mg
4. RH038 Ethinylestradiol/Levonorgestrel + Ferrous Fumarate
   Ethinylestradiol/Levonorgestrel Tablet + Placebo (Ferrous Fumarate Tablet) 30mcg/150mcg + 75mg
5. RH049 Desogestrel/Ethinylestradiol + Placebo
   Desogestrel/Ethinylestradiol Tablet + Placebo Tablet 150mcg/30mcg + 0mcg
6. RH057 Levonorgestrel Tablet, Film-coated 0.03mg (under assessment at the time of the inspection)

Additional products covered by this desk assessment:

RH074

Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Meaning</th>
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<tr>
<td>API</td>
<td>Active pharmaceutical ingredient</td>
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<td>BMR</td>
<td>Batch manufacturing record</td>
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<td>BPR</td>
<td>Batch production record</td>
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<td>CAPA</td>
<td>Corrective and preventive action</td>
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<tr>
<td>CC</td>
<td>Change control</td>
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<tr>
<td>GMP</td>
<td>Good manufacturing practices</td>
</tr>
<tr>
<td>NC</td>
<td>Non conformity</td>
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<tr>
<td>NRA</td>
<td>National regulatory agency</td>
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<tr>
<td>PQR</td>
<td>Product quality review</td>
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<td>PQS</td>
<td>Pharmaceutical quality system</td>
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<td>QA</td>
<td>Quality assurance</td>
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<td>QC</td>
<td>Quality control</td>
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<td>QCL</td>
<td>Quality control laboratory</td>
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<td>QMS</td>
<td>Quality management system</td>
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<td>QRM</td>
<td>Quality risk management</td>
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<tr>
<td>RA</td>
<td>Risk assessment</td>
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<td>RCA</td>
<td>Root cause analysis</td>
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<td>SOP</td>
<td>Standard operating procedure</td>
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<td>SMF</td>
<td>Site master file</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:
Reviewed and considered acceptable.

b) Site master file (SMF):
The SMF dated 13 February 2019, was reviewed and is considered acceptable.

c) List of regulatory inspections performed in the last 5 years and their outcome:
The company declared that the site was inspected by the following authorities:
2. USFDA (OSD) – Jan 2018. In compliance
3. USFDA (Injectable) – June 2018. In compliance
4. Health care Inspectorate, Netherlands – April 2018. In compliance
5. Taiwan FDA – June 2017. In compliance
7. USFDA (OSD) – October 2014. In compliance
8. Health care Inspectorate, Netherlands – April 2014. In compliance

d) List of all the products and dosage forms manufactured on-site:
The list of products manufactured on site is acceptable and does not raise particular concerns with
regards to potential cross-contamination. In the injectable facility, only medroxyprogesterone
acetate injectable suspension is manufactured. In the OSD division, only tablets containing female
generic hormones for human use are being produced at the site. It did not include any veterinary
products.

e) Most recent product quality review(s) (PQR)(s) of the concerned WHO product(s):
No PQR is available as of yet for the RH074 product as only regulatory batches were manufactured.
PQRs were submitted for the prequalified OSD products, namely: RH031, RH032, RH037, RH038,
RH049 and RH057. The following PQRs were reviewed:
-For RH057: individual PQRs were submitted for the bulk product and for different finished
product codes of the Product Levonorgestrel Tablets 0.03 mg. The PQR for the product destined to
the Rwanda and Papua New Guinea market was reviewed. It was for the review period of January
2017-December 2017. It included a review of OOS, OOT, CPPs, in-process controls and finished
product results, stability data, change controls, validation, returns, complaints, recalls, regulatory,
review of open items for the previous PQR. It did not include a review of the utilities. The PQR for
the bulk product was also reviewed and include supplementary sections (review of starting
materials and packaging materials, review of the qualification status of relevant equipment and
facility/utility, quality/technical agreements). This was considered acceptable overall.
f) **Batch manufacturing and packaging record(s), including the analytical part, for the most recently released batch of relevant product(s):**

An executed batch record was provided for the medroxyprogesterone acetate batch, manufactured 08 2018. It was released on 21/09/2018 and the quantity manufactured was 1,489 packages of 25 vials each (37,225 vials in total). It covered manufacturing by autoclave sterilization in a 250 L CIP vessel using sterile API (gamma irradiated by the supplier). This is close to the final commercial batch size of 50L/41,666 vials that is proposed for the commercial manufacturing process for WHO (same size as used for the biostudy/stability and process validation studies).

g) **Recalls in the past three years related to products with quality defects:**

The company provided a declaration on the absence of recalls in the last 3 years for PQ products. There were 2 class III (voluntary) recalls on the US market. Adequate corrective and preventive actions were made further to those recalls.

i) **Confirmation by the senior quality assurance representative that a full self-inspection or external audit dedicated to the product(s) has been performed and all matters dealt with:**

The declarations were provided for all WHO prequalified products. It stated that self-inspections are conducted every 6 months and all issues reported to senior management were handled through the QMS and closed. This is considered acceptable.

j) **Copy of any warning letter, or equivalent regulatory action, issued by any authority to which the site provides or has applied to provide the product:**

A declaration was provided that no warning letter or equivalent regulatory action was taken by any regulatory authority for products supplied by Mylan.

k) **Out-of-stock situations:**

The company submitted a declaration that out-of-stock events for medroxyprogesterone acetate injectable suspension USP 150 mg/mL shall not be more than 0.1%. It also briefly described measures taken to avoid out of stock situations.

This declaration was also submitted for the OSDs RH031, RH032, RH037, RH038, RH049 and RH057 and considered acceptable.

l) **Additional documents submitted:**

Not applicable.

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<tr>
<th>Part 5</th>
<th>Conclusion – Desk assessment outcome</th>
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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, Sarkhej 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.
<table>
<thead>
<tr>
<th>Part</th>
<th>List of guidelines referenced in this inspection report</th>
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</table>
Short name: WHO GPPQCL guidelines or WHO TRS No. 957, Annex 1

Short name: WHO TRS No. 957, Annex 2

Short name: WHO TRS No. 961, Annex 6
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

Short name: WHO TRS No. 961, Annex 7
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

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

Short name: WHO TRS No. 943, Annex 3
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/

   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

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


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

*Short name: WHO TRS No. 996, Annex 10*