

29th November 2018

To,
The Ministry of health
Kuala Lumpur
Malaysia

Subject: Letter of justification on Manufacturing Site address appearing on the TGA & MHRA GMP for Cipla Indore Site.

Dear Sir,

This is regarding registration of the product Ipratropium pressurised Inhalation BP (20 mcg/dose) submitted from Manufacturing site Indore unit II. We have submitted the GMP certificate issued by MHRA and TGA for the manufacturing site and mentioned address on GMP certificate along with WHO GMP is as below.

GMP Certificate	Mentioned address
TGA-Australia	Cipla Limited, Plot no. 9, 10 & 15, Pharma Zone, Phase II, Sector III, Indore Special Economic zone. Pithampur, District- Dhar, MP - 454775, India
MHRA- UK	Cipla Limited, Plot no. 9, 10 & 15, Indore Special Economic zone. Phase II, Pithampur, District- Dhar, MP - 454775, India
WHO GMP/COPP	Cipla Limited, Plot no. 9 & 10, Pharma Zone, Phase II, Indore SEZ, Pithampur, MP - 454775, India

1. Justification for Sector III appearing on TGA GMP.

GMP certificate issued by TGA states the address as "Cipla Limited, Plot no. 9, 10 & 15, Pharma Zone, Phase II, Sector III, Indore Special Economic zone. Pithampur, District- Dhar, MP - 454775, India." whereas the WHO-GMP for the manufacturing site states the address as "Cipla Limited, Plot no. 9 & 10, Pharma Zone, Phase II, Indore SEZ, Pithampur, MP - 454775, India." We would like to inform that Cipla Indore manufacturing site plot 9 & 10 is located in phase II of Indore special economic zone (ISEZ). The phase II of ISEZ is in the sector III. Therefore, TGA GMP has sector III in the manufacturing site address.

2. Justification for plot no. 15 appearing on the GMP certificate by MHRA.

GMP certificate issued by MHRA states the address as "Cipla Limited, Plot no. 9, 10 & 15, Indore Special Economic Zone, Phase II, Pithampur, District- Dhar, MP-

Cipla Ltd., R&D Centre, LBS Marg, Vikhroli (W), Mumbai - 400 083, India.

Phone: +91 22 25756000, 25756300 • Fax: +91 22 25785298 • Email: globalra@cipla.com

Cipla Ltd. Regd. Office Cipla House, Peninsula Business Park, Ganpatrao Kadam Marg, Lower Parel, Mumbai - 400 013
Phone +91 22 24826000 Fax +91 22 24826120 Website www.cipla.com Corporate Identity Number L24239MH1935PLC002380

454775, India. whereas the WHO-GMP for the manufacturing site states the address as "Cipla Limited, Plot no. 9 & 10, Phase II, Indore Special Economic Zone, Pithampur, District- Dhar, MP- 454775, India." We would like to inform that Plot No. 15 is adjacent to plot no. 9 & 10 and hence it appears on site master file along with plot no. 9 & 10. The site address on the MHRA Certificate is based on the address mentioned on the Site Master File which contains all plots number (9, 10 & 15) of Cipla Indore location (at Pharma Zone). Plot 15 is for future expansion and now only plot 9 & 10 is operational. Therefore, GMP Certificate and COPP states only plot no 9& 10 while address on MHRA certificate. includes all the plots i.e 9, 10 and 15 as per site master file

3. Justification for Pharma Zone that is mentioned on the COPP

The company is situated in Indore Special Economic Zone and Indore Special Economic Zone is further divided in three Zones, Apprial Zone, Pharma Zone and Miscellaneous Zone. Cipla Indore is located in Indore Special Economic Zone, Pharma Zone and the same is mentioned in COPP. However the same was not mentioned on GMP certificate, although the pharma zone is appearing on covering page of the GMP certificate

Hope the above justification suffice the query and provide your kind approval.

Thanking you,

For Cipla Ltd.,



Sheetal More
Regulatory responsible person

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29th October 2018

To,
The Ministry of health
Kuala Lumpur
Malaysia

Subject: Declaration letter for Description of Product Ipratropium Pressurised Inhalation BP (20mcg/dose)

Dear Sir,

This is regarding registration of the product Ipratropium Pressurised Inhalation BP (20 mcg/dose) submitted from Manufacturing site Indore unit II.

Our Ipratropium Pressurised Inhalation BP is a pressurized metered-dose aerosol packaged in an aluminium can with a suitable metering valve and a polypropylene actuator.

As per ICH Q6A guidelines, the “description” should cover the following:

A qualitative description of the dosage form should be provided (e.g., size, shape, and colour). If any of these characteristics change during manufacture or storage, this change should be investigated, and appropriate action taken. The acceptance criteria should include the final acceptable appearance. If colour changes during storage, a quantitative procedure may be appropriate.

For Ipratropium Pressurised Inhalation BP, the description of dosage form needs to cover appearance of container closure system along with formulation description since both these form the dosage form i.e. pressurised metered dose inhaler.

Although description of container closure system can be seen visually by a chemist, same is not possible for inside content. In order to actually evaluate description of the inside contents i.e. formulation, the chemist needs to cut open the can (as per specialized technique given in method of analysis). As the product contains propellant which has boiling point of -26°C, the propellant evaporates on opening of the can. Hence the product description which a chemist can see is only colourless solution - which is of the drug substance and other excipients. Considering the same, the description of the product is stated to reflect the product description as visible to the QC chemist on opening of the can.

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Hence the Product description is kept as 'A one piece filled metal container fitted with a valve with plastic stem and printed with product identification code, batch number and container number. On visual examination, there should be no sign of physical damage such as dents, bulged containers, bent valve stem, and uneven crimping. Printing details should be legible. Colourless solution is obtained after opening the container'

Kindly consider the same.

Thanking you,

For Cipla Ltd.,



Sheetal More

Regulatory responsible person

