



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring, MD 20993

MEMORANDUM

**DATE:** March 19, 2020

**FROM:** Francis Godwin, Director  
Office of Manufacturing Quality  
Office of Compliance  
Center for Drug Evaluation and Research

**THROUGH:** Carmelo R. Rosa, Director for  
Division of Drug Quality I  
Office of Manufacturing Quality  
Office of Compliance  
Center for Drug Evaluation and Research

**TO:** John E. Verbeten, Acting Director  
Division of Import Operations  
Office of Enforcement and Import Operations  
Office of Operations  
Office of Regulatory Affairs

**SUBJECT:** Recommendation to Revise Import Alert (IA) 66-40

Francis  
Godwin -S

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DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=Francis Godwin -S, 0.9.2342.19200300.100.1.1=2000376143  
Date: 2020.03.19 15:11:50 -04'00'

Maan S.  
Abduldayem -S

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DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2000331842, cn=Maan S. Abduldayem -S  
Date: 2020.03.19 15:07:59 -04'00'

CDER, Office of Compliance (OC), Office of Manufacturing Quality (OMQ), Division of Drug Quality I (DDQ I) recommends revision of IA 66-40 to include future shipments of active pharmaceutical ingredients manufactured by the firm referenced below. Our office will request removal of the firm from the IA if we are satisfied that the manufacturer has resolved the conditions that gave rise to the appearance of the deviation. In most instances, this will require a FDA re-inspection.

**Manufacturer:** IPCA Laboratories, Ltd.  
P.O. Box No. 33 Village Sejavta  
Ratlam (Madya Pradesh) 457002  
India  
FEI: 3002807297

**Products:** All drugs and Drug Products except<sup>1</sup>:

<sup>1</sup> Import/Export division suggested the use of bracket for each drug

- Hydroxychloroquine Sulfate: product code 62[ ] [ ] 29
- Chloroquine Phosphate: product code 61A[ ] [ ] 06

**Charge:** The article is subject to refusal of admission pursuant to Section 801(a)(3) of the Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 381(a)(3), in that the methods and controls used in their manufacture do not appear to conform to current good manufacturing practice within the meaning of Section 501(a)(2)(B) of the Act, 21 U.S.C. § 351(a)(2)(B).

FDA conducted an inspection of this firm from July 14-18, 2014. The inspection revealed many significant deviations from CGMP requirements for the manufacture of drugs. These deviations cause the drugs manufactured at IPCA Laboratories Ltd to appear to be adulterated within the meaning of section 501(a)(2)(B) of the Act in that the methods used in, or the facilities or controls used for, their manufacture, processing, packing, or holding do not conform to, or are not operated or administered in conformity with, CGMP requirements. Significant CGMP violations include<sup>2</sup>:

- Data integrity issues - original results processed and printed out; however, administrator privileges were used to re-integrate the injections and report passing results.
- Data collected from in June-July of 2013 using instrument GC#'s 052 and 202 (2 of (b) (4) total GCs) encountered: manipulation of PC time and date setting (using admin. privilege), manipulation of integration parameters to achieve passing results, aborting ongoing samples analyses and deleting the raw data files, and overwriting previously collected raw data files (initial raw data file not available for review).

**May 2017 - Update Information to justify the revision of import alert memo for drug carved out**

On December 15, 2014, OMQ approved the import alert with some drugs carved out<sup>3</sup>. On January 29, 2016, warning letter no. 320-16-07 was issued. (b) (7)(A)

(b) (7)(A)

<sup>2</sup> For detail refer to the original import alert memo signed by OMQ Office Director

<sup>3</sup> Import alert date published: 01/22/2015

(b) (7)(A)

(b) (7)(A)

(b) (7)(A)

On May 1 and May 12, 2017, OMQ/DDQI received update drug shortage assessment from CDER Drug Shortage Team. CDER Drug Shortage Team indicated that they no longer have drug shortage concerns with the following drugs that were initially excluded from Import Alert 66-40: Sulfamethoxazole, Trimethoprim, Ondansetron, Hydroxychloroquine Sulfate and Propanol Hydrochloride. DSS still had concern about Chloroquine Phosphate, therefore this product remained excluded from IA 66-40.

**March 2020 - Update Information to justify the revision of import alert memo for drug carved out**

Due to the outbreak of the COVID-19, caused by a novel coronavirus, around the world including the United States, OMQ received a request from DSS to add Hydroxychloroquine Sulfate as a carve out drug. The request is an action to alleviate a potential shortage of the drug for the treatment of the coronavirus caused COVID-19. Therefore, the revised IA 66-40 will include all drugs and drug products manufactured by this facility except: Hydroxychloroquine Sulfate (product code 62[[[29)]; Chloroquine Phosphate (product code 61A[[[06]).

If you have any questions, please contact Rafael Arroyo at [rafael.arroyo@fda.hhs.gov](mailto:rafael.arroyo@fda.hhs.gov) or at (301) 796-4839.

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Date: 2020.03.19 15:12:39 -04'00'

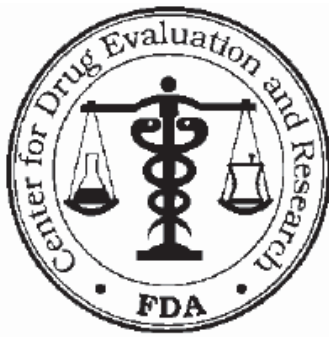
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Francis Godwin  
Director  
Office of Manufacturing Quality  
Office of Compliance  
Center for Drug Evaluation and Research

LIST OF ATTACHMENTS

Attachment 1 – DSS consult email

Attachment 2 – Original import alert approved with drugs carved out



**DEPARTMENT OF HEALTH & HUMAN SERVICES**  
**Public Health Service**  
**Food and Drug Administration**  
**Center for Drug Evaluation and Research**

**MEMORANDUM**

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**DATE:** March 20, 2020

**FROM:** **Francis Godwin**, Director  
Office of Manufacturing Quality  
Office of Compliance  
Center for Drug Evaluation and Research

Rick L. Friedman -S  
Digitally signed by Rick L. Friedman -S  
Date: 2020.03.22 22:43:12 -04'00'

**THROUGH:** **Carmelo Rosa**, Director  
Division of Drug Quality I  
Office of Manufacturing Quality  
Office of Compliance  
Center for Drug Evaluation and Research

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2 cn Carmelo R. Rosa -S  
Date: 2020.03.20 16:42:51 -04:00

**TO:** **John Verbeten**, Director  
Division of Import Operations  
Office of Enforcement and Import Operations  
Office of Operations  
Office of Regulatory Affairs

**SUBJECT:** Recommendation to Revise Import Alert (IA) 66-40

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CDER, Office of Compliance (OC), Office of Manufacturing Quality (OMQ) recommends revision of IA 66-40 to include future shipments of drugs manufactured by the firm referenced below. Our office will request removal of the firm from the IA when we are satisfied that that the manufacturer has resolved the conditions that gave rise to the appearance of the violation. In most instances, this will require an FDA reinspection.

**Manufacturer (finished products):** IPCA Laboratories Limited  
Plot 65 & 99, Danudyog Industrial Estate, Piparia  
Silvassa 396 230 (Union Territory of Dadra & Nagar Haveli)  
India  
FEI: 3005977675

**Product:** All Drugs and Drug Products except<sup>1</sup>:

- Hydroxychloroquine Sulfate tablets: (b) (4) A-Malarial (Product code 62L[[[29)

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<sup>1</sup> Imports/Export division suggested the use of brackets for each drug because they do perform a wider search

**Manufacturer (finished products):** IPCA Laboratories Ltd

Location: 1 Pharma Zone, SEZ Phase II, Sector 3  
District Dhar, Pithampur  
Madhya Pradesh, India  
FEI: 3007574780

**Product:** All Drugs and Drug Products, except

- Hydroxychloroquine Sulfate tablets: (b) (4) A-Malarial (Product code 62L[[[29)

**Charge:** The articles are subject to refusal of admission pursuant to Section 801(a)(3) of the Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 381(a)(3), in that the methods and controls used in their manufacture do not appear to conform to current good manufacturing practices (CGMP) within the meaning of section 501(a)(2)(B) of the Act, 21 U.S.C. § 351(a)(2)(B).

FDA inspected IPCA Laboratories located in Pithampur and IPCA Laboratories located in Piparia, India in October and December 2014, respectively. The inspections revealed significant deviations from CGMP requirements for the manufacture of drugs. These deviations cause the drugs manufactured at IPCA Laboratories Ltd located in Pithampur and Piparia, India to appear to be adulterated within the meaning of section 501(a)(2)(B) of the Act in that the methods used in, or the facilities or controls used for, their manufacture, processing, packing, or holding do not conform to, or are not operated or administered in conformity with, CGMP requirements. Examples of CGMP violations include:

- Data integrity issues. The investigators found instances where chromatograms were generated after several trial injections were performed. The investigator found several repeated chromatographic injections with no justification.
- Equipment audit trail issues. During the review of the firm's electronic GC chromatography data audit trails, the investigators noted what appeared to be a laboratory practice of overwriting and deleting raw data files. There are four examples listed in the Form FDA 483 that were collected during the inspection.
- Computer control issues. Appropriate controls are not exercised over computers or related systems to assure that change in master production and control records or other records are performed only by authorized personnel. The investigator documented that one o (b) (4) GC instruments (Perkin Elmer #072) is not equipped with an audit trail feature that rec the date and time of actions it creates, modifies, or delete electronic records.

Both sites are classified OAI. OMQ is recommending that all drug products produced by the referenced firms, except the drug product listed above in this recommendation for both IPCA facilities, be added to IA-66-40.

**March 20, 2020 Updated Information**

**Justification for the Updating Import Alert 66-40 to Carve Out Hydroxychloroquine Sulfate Tablets**

Due to the outbreak of the COVID-19, caused by a novel coronavirus around the world, including the

United States, OMQ received a request from DSS to add Hydroxychloroquine Sulfate tablets as a carve out drug product. The request is an action to alleviate a potential shortage of the drug for the treatment of the coronavirus caused COVID-19. Therefore, the revised IA 66-40 will include all drug and drug products manufactured at both facilities except: Hydroxychloroquine Sulfate tablets (product code 62[ ] [ ]29).

If you have any questions, please contact Rafael Arroyo at [rafael.arroyo@fda.hhs.gov](mailto:rafael.arroyo@fda.hhs.gov) or at 301-796-4839.

Sincerely,

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Francis Godwin  
Director  
Office of Manufacturing Quality  
Office of Compliance  
Center for Drug Evaluation and Research





**DATE:** March 23, 2020

**TO:** Office of Regulatory Affairs (ORA)  
Office of Operations  
Office of Enforcement and Import Operations  
Division of Import Operations

**FROM:** Tara P. Turner, Consumer Safety Officer  
CDER/Office of Compliance  
Office of Drug Security, Integrity, and Response  
Division of Global Drug Distribution and Policy  
Imports Exports Compliance Branch (IECB)

**SUBJECT:** Recommendation to Revise Import Alert #66-40, "Detention Without Physical Examination of Drugs From Firms Which Have Not Met Drug GMPs" (CMS Case #606164)

This memo responds to the CDER Office of Compliance (OC), Office of Manufacturing Quality (OMQ), Division of Drug Quality I's (DDQ I's) memo of March 20, 2020 recommending revision of Import Alert (IA) #66-40, "Detention Without Physical Examination of Drugs From Firms Which Have Not Met Drug GMPs" to **exclude** the following finished drug products manufactured by the following firms:

1. IPCA Laboratories Limited, Piparia site (FEI: 3005977675)
  - Hydroxychloroquine Sulfate tablets: (b) (4) A-Malarial (Product code 62L[ ][ ]29)
2. IPCA Laboratories Ltd, Pithampur site (FEI: 3007574780)
  - Hydroxychloroquine Sulfate tablets (b) (4) A-Malarial (Product code 62L[ ][ ]29)

The initial Import Alert 66-40 for the above-referenced firms was issued in March 2015. Due to shortage concerns, the following drugs were carved out from the initial Import Alert: Hydroxychloroquine Sulfate Tablets and Propranolol Hydrochloride Tablets manufactured at the IPCA Piparia site. In June 2015, the Import Alert was revised to also carve out Hydroxychloroquine Sulfate Tablets manufactured at the IPCA Pithampur site.

A May 2017 reassessment by the Drug Shortage Staff indicated there were no longer drug shortage concerns with Hydroxychloroquine Sulfate Tablets and Propranolol Hydrochloride Tablets. Thus, in June 2017, they were added to the Import Alert.

In March 2020, due to the outbreak of the COVID-19, caused by a novel coronavirus around the world, including the United States, OMQ received a request from DSS to add Hydroxychloroquine Sulfate tablets as a carve out drug product. The request is an action to alleviate a potential shortage of the drug for the treatment of the illness caused by COVID-19. Therefore, the revised IA 66-40 will include all drug and drug products manufactured at both facilities **except**: Hydroxychloroquine Sulfate tablets (product code 62[ ][ ]29).

CDER IECB supports these revisions.