DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857 CDER-OC-OMQ-International483Response@fda.hhs.gov	02/03/2025-02/07/2025
	FEI NUMBER 3003560263

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Dr. K. Suresh Babu, Head - Corporate Quality and Regulatory Affairs

FIRM NAME	STREET ADDRESS
Hikal Limited	72 & 82/A Kiadb Industrial Area
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Jigani, Anekal, Bengaluru, Karnataka, 560105, India	API and Intermediate Manufacturer

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

The observations noted in this Form FDA-483 are not an exhaustive listing of objectionable conditions. Under the law, your firm is responsible for conducting internal self-audits to identify and correct any and all violations of the quality system requirements.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED

OBSERVATION 1

Complaints are not adequately investigated, and appropriate follow ups are not performed. Specifically,

Your firm has received numerous complaints of foreign matter/material contamination in released batches of API. The chart below details the varied and continuous nature of received complaints of foreign matter contamination in US distributed product/API used in production of Drug Product distributed in the US:

Complaint No.	Date received	Date closed	Product	Batch Number	Manufacturing date	Description of the complaint
MC-026/19	09.10.2019	02.01.2020	(b) (4)			1) Excrements on lid of the (b) (4) drums 2) Black foreign particle on (b) (4) (b) (4) bags within the drum. 3) shrink wrap not applied to drums, mixed batches on single pallets 4) (b) (4) formation (b) (4)
MC-033/19	18.12.2019	04.04.2020				Foreign material contamination (black particles, potentially metal contamination, below LOD of detectors)
MC-012/20	06.05.2020	05.11.2020				Foreign material contamination (b) (4) particles, (b) (4) (b) (4) black particles).
MC-014/20	06.05.2020	05.11.2020				Foreign material contamination (b) (4) particulates (b) (4) (b) (4) black particles).

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MC-020/20	12.06.2020	20.08.2020	(b) (4)	Foreign matter contamination (b) (4) (b) (4) potentially (b) (4) drum lid material)
MC-024/20	20.08.2020	03.03.2021		Foreign matter contamination (metallic and non-metallic)
MC-028/20	14.10.2020	25.12.2020		Foreign matter contamination (b) (4)
MC-003/21	02.02.2021	04.05.2021		Foreign matter contamination (b) (4)
MC-004/21	05.02.2021	25.06.2021		Foreign matter contamination (hair, (b) (4) fibers)
MC-006/21	18.02.2021	02.08.2021		Foreign material contamination (b) (4) Black particles).
MC-009/21	12.04.2021	02.08.2021		Foreign matter contamination in tablet (b) (4) particles).
MC-010/21	17.06.2021	03.09.2021		Foreign matter contamination in tablet (b) (4)
MC-030/21	12/7/2021	4/20/2022		Foreign matter contamination (b) (4) (b) (4) particles)
MC-001/22	18.01.2022	3/14/2022		Foreign matter contamination (black particles)
MC-002/22	19.01.2022	3/28/2022		(b) (4) bag found in bottom of drum
MC-010/22	02.05.2022	12/2/2022		Black particles in drum container
MC-015/22	08.06.2022	5/2/2023		Foreign particle found in the material, potentially metal contamination below the limit of metal detector.
MC-023/22	25.08.2022	5/2/2023		Foreign matter contamination (hair, metal particles)

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MC-024/22	27.08.2022	11/28/2022	(b) (4)	After (b) (4) of (b) (4) (b) (4) USP through (b) (4) extraneous material (b) (4) pieces) observed (b) (4) (b) (4)
MC-027/22	28.09.2022	5/2/2023		Foreign matter contamination (hair).
MC-029/22	07.11.2022	3/30/2023		Foreign matter contamination. (head of cable/zip tie found in product container)
MC-030/22	08.11.2022	5/3/2023		Dark spot found in one drum
MC-031/22	10.11.2022	07.02.2023		Foreign matter contamination (b) (4) found in between the drum)
MC-036/22	24.11.2022	8/21/2023		Foreign matter contamination (Black Specs)
MC-004/23	26.01.2023	02.05.2023		Foreign matter contamination (Metal particles and hair in tablet)
MC-010/23	10.03.2023	11.05.2023		Foreign matter contamination (whole (b) (4) Bolt found in drum, in bulk material)
MC-012/23	13.03.2023	10.10.2023		Foreign matter contamination (Metal and hair particles in tablet)
MC-039/23	03.10.2023	11.12.2023		Foreign material contamination (b) (4) bag used to collect area cleaning waste, used as primary packaging bag)
MC-043/23	30.11.2023	27.02.2024		Foreign matter contamination (fibers, black particles
MC-044/23	01.12.2023	14.05.2024		Foreign matter contamination (Live insect was detected inside the sealed container.)
MC-007/24	18.03.2024	19.06.2024		Foreign matter contamination (Hair, shredded fiber, Drum lid piece, (b) (4) piece etc.,)
MC-010/24	06.04.2024	12.08.2024		(b) (4) Scoop found in container No. (b) (4) of (b) (4)

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MC-019/24	18.07.2024	09.12.2024	(b) (4)	Black metal particles observed by the customer
MC-020/24	01.08.2024	11/12/2024		Detection of hair fibers and metal particles in (b) (4) tablets by the customer.
MC-028/24	9/25/2024	1/31/2025		(b) (4) Cap found by customer during (b) (4) of (b) (4) USP.
MC-029/24	10/2/2024	11/4/2024		A piece of (b) (4) found by customer, inside the container # (b) (4) from Batch # (b) (4)
MC-030/24	10/14/2024	06.12.2024		Black spots and (b) (4) fiber-like material found by customer .

Foreign matter contamination has been steadily reported to your firm, by customers, since the last FDA inspection (conducted from 7/29/2019 to 8/2/2019).

OBSERVATION 2

Out-Of-Specification (OOS) results are routinely invalidated, without sufficient supporting evidence or scientific justification of the root cause. Specifically,

Of 92 invalidated OOS results relating to US distributed product, 24 investigations were invalidated without establishing a root cause, with conforming retest results accepted and batches released.

OBSERVATION 3

Appropriate maintenance and calibration of critical equipment is not performed. Specifically,

There is no assurance that API and intermediate drug products manufactured in your firm's Unit (b) (4) production blocks (b) (4) are free from metal (b) (4) contamination. Your firm has received repeated and continuous complaints regarding potential metal contamination in APIs. During the inspection it was determined that your firm does not routinely challenge the ability of metal detectors at Unit (b) (4) production blocks, to detect (b) (4) contamination in APIs. Furthermore, it was observed that your firm's Unit (b) (4) site, does not possess certified (b) (4) challenge pieces (b) (4) The Unit (b) (4) site manufactures the following APIs for US distribution/use in use in Drug Product distributed in the US.

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OBSERVATION 4

Written procedures are deficient. specifically

A. Your firm's vendor qualification procedure, CQA01002-01, indicates that vendors are assessed on the number of consecutive rejections encountered during incoming material inspection. However, no provision for vendors that provide materials that are identified as deficient later in the manufacturing process, or after distribution. For example, your firm received multiple complaints regarding (b) (4) (b) (4) drums and (b) (4) lids, supplied by (b) (4) An on-site audit of the vendor was performed by your firm's personnel in April 2024, to which the vendor responded with a bevy of procedural changes, facility improvements and training. However, complaints related to drum fibers and pieces of the lids, continued to occur. (b) (4) maintain a "A" rating with a" zero-rejection rate", despite the continuous nature of received complaints. To date, alternate vendors have been qualified, however, according to your firm's management team, (b) (4) (b) (4) provide approximately greater than (b) (4)%, however, an exact percentage could not be verified.

OBSERVATION 5

Back-up data is not appropriately protected from unauthorized access, manipulation or deletion. Specifically,

During a walkthrough of your firm's microbiology laboratory, a "qc" folder located on the server (IP: 172.21.21.25) contained a folder titled "CHROMELEON 6.8 BACKUP BEFORE MIGRAGTION". The folder and contained filed had no file protections/access controls. a folder titled "GC-213", was fully accessible and able to be deleted while logged in (b) (6) Senior Manager, Microbiology. although the deletion process was aborted to preserve data. Prior to observation during the microbiology laboratory walkthrough, your firm's IT personnel were seemingly unaware that the Chromeleon backup data was saved to User file folders and not the designated IT Folder/Backup System. The backup folder contained equipment specific folders with data from Gas Chromatograph (GC) and Liquid Chromatograph (LC): (b) (4) (b) (4)

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OBSERVATION 6

Incidents related to computerized systems that could affect the quality of intermediates or APIs are not recorded and investigated. Specifically,

Your firm's (b) (4) processing equipment (b) (4) packing) is controlled by a Process Logic Controller (PLC) in conjunction with a Human Machine Interface (HMI-16). events that are encountered generate a temporary notification visually on the HMI, and per (b) (4) require Production personnel to contact the engineering department. However, neither the computerized system/software used to manage the process, nor the written procedure/production batch record require any documentation of the events encountered. Upon request, your firm could not provide a single documented instance of any of the 37 events, requiring engineering department notification, defined in (b) (4) since installation of the system. There is no mechanism to assess the adequacy of the (b) (4) processing.

***DATES OF INSPECTION**

02/03/2025 (Mon), 02/04/2025 (Tue), 02/05/2025 (Wed), 02/06/2025 (Thu), 02/07/2025 (Fri).

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgment, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."