DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
11155 Dolfield Boulevard, Suite 117 Owings Mills, MD 21117 (410)779-5455 Fax:(410)779-5707 ORAPHARM1_RESPONSES@fda.hhs.gov	7/18/2022-7/22/2022
	FEI NUMBER 3011585184

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Vijay Ramanavarapu, President

FIRM NAME	STREET ADDRESS
Granules Pharmaceuticals Inc	3701 Concorde Pkwy
CITY, STATE, ZIP CODE, COUNTRY Chantilly, VA 20151-1126	TYPE ESTABLISHMENT INSPECTED Drug 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.

DURING AN INSPECTION OF YOUR FIRM I OBSERVED:

OBSERVATION 1

The responsibilities and procedures applicable to the quality control unit are not in writing and fully followed.

Specifically,

A. SOP: GP-026 Rev. No. 04 effective date 7/30/2021, entitled, "Incident Report and Investigation Writing" pg 17 of 18, Appendix 3 reflects that Management is to be notified of "Major" incident. However, examples of this SOP not being followed are:

i. IR Form 21-176 that occurred on 11/22/2021 during the (b) (4) process involving Dexmethylphenidate HCl ER Capsules Lot GPC211003 was due to an operator noticing the (b) (4) Temperature to be out of range ((b) (4)) at -7 degrees Celsius. On page 3 of 4, the initial assigned Incident Severity Code is reflected as "Major," however, the Management Notification Requirement reflects "No."

ii. IR Form 22-002 that occurred on 1/5/2022 in Room 129 because Dispensing operators (b) (6) and (b) (6) performed a (b) (4) cleaning instead of a (b) (4) cleaning between dispensing of excipients for two separate products, Trospium Chloride ER capsules – seal coating (lots GPC220005-GPC220008) and Potassium Chloride ER Tablets 750 mg (Lots GPC211122-GPC211123, (b) (4) tablets). On page 2 of 3, the initial assigned Incident Severity Code is reflected as "Major," however, the Management Notification Required reflects "No."

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	William J Leonard, Investigator X William J Leonard Investigator Signed By: William J. Leonard -S Date Signed: 07-22-2022 12: 0:38	7/22/2022

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OBSERVATION 2

Written production and process control procedures are not followed in the execution of production and process control functions and documented at the time of performance.

Specifically,

During the inspection of documentation and logbooks found a number of examples where procedures were not followed:

a. Warehouse Capsule Storage Temperature and Humidity Monitoring logs for the period from November 2012 to February 2022 reported a failure to meet humidity control limits of 35-65% RH on the following dates: 11/16/21, 01/26/22, 01/27/22, 01/31/22, 02/07/22 and 02/14/22. The entries were reviewed by a quality assurance representative and no action was taken to correct the out of limit condition.

b. Equipment Use Logbook entries for "Type of Cleaning" were missing for the following equipment on dates listed below:

1. The (b) (4) Solution Tank GP-0055 on 04/06/22, 06/11/22 and 06/24/22.
2. The (b) (4) Moisture Analyzer GP-1196 on 06/11/22.

c. Balance Verification Logbooks for the (b) (4) Balance GP-0119 and the (b) (4) (b) (4) GP-1141 lack a traceable reference to the certified weight set used in the (b) (4) performance check.

d. Cleaning Procedure for Drums, Pails, Pallets, Hi-Lo, and Pallet Jacks GPM-074 calls for the cleaning of containers used to hold drug components. The procedure does not require a record of the cleaning operation or traceable status labels indicating who and when cleaning occurred. These devices are routinely used in the production of drug products at the facility.

e. Warehouse Temperature and Humidity Monitoring logbook ID G-WH-22-0042 was put in service without being issued by quality assurance as required in SOP QA-006 Logbook/notebook Request, Issuance and Archival.

This observation is a repeat of Observation 1 from the January 2022 inspection.

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OBSERVATION 3

Equipment used in the manufacture, processing, packing or holding of drug products is not of appropriate design to facilitate operations for its intended use.

Specifically,

a. The firm manufactures the pharmaceutical intermediate (b) (4) w/w with the aid of a (b) (4), equipment ID GP-0054. Review of the Qualification Protocol #EV15008, approved on 06/22/2016 for this (b) (4) revealed a single trial of (b) (4) to demonstrate the performance range of (b) (4) degrees celsius at (b) (4) set points. The (b) (4) executed (b) (4) w/w exhibit batches (b) (4), and (b) (4) supporting (b) (4) utilize (b) (4), equipment ID GP-0054 with a temperature range of (b) (4) degrees over at least (b) (4). (b) (4), equipment ID GP-0054 is not qualified to operate at this temperature for at least (b) (4)

b. Sampling of all drug components is performed in the (b) (4) Model (b) (4) (b) (4), GP-1270 located in the warehouse following SOP MM-018. Section 5.4-5.7 describes the process of starting the (b) (4) by entering the (b) (4) and turning the system switch on. The procedure then states sampling activities may start immediately based on the (b) (4) Review of the Operation Qualification Protocol Document No. K3D/534/OQ/DFB/001 page (b) (4) of (b) (4) calls for an Air borne particles test to assess ISO class requirements. The test requires the user to switch on the unit then wait (b) (4) to stabilize. The procedure for routine use does not follow the requirement to wait (b) (4) (b) (4) before use.

OBSERVATION 4

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Procedures designed to prevent objectionable microorganisms in drug products not required to be sterile are not established.

Specifically,
Qualification of the (b) (4) systems installed and operating in buildings 3701 and 3725 did not demonstrate a design suitable to prevent objectional microorganisms in the following ways:
1. There is no record of selective growth promotion for organisms other than coliforms, that represent risk to the product and process.
2. There is no record in the Performance Qualification ((b) (4)) to indicate (b) (4) samples collected from (b) (4) typically used to deliver (b) (4) to each process in the building 3725 (b) (4) .
3. (b) (4) of the Performance Qualification for building 3725 did not demonstrate (b) (4) (b) (4) of passing total organic carbon results as required in the protocol.
4. On 06/23/22, building 3701 (b) (4) system GP-0184 went out of service and the mitigation included the collection and use of (b) (4) obtained from building 3725 and transported to building 3701 and used within (b) (4) . There is no data to support the (b) (4) transported to 3701 for use in process and production of drugs meets the (b) (4) quality specification (b) (4) after collection. The (b) (4) produced in buildings 3701 and 3725 is used to produced drug products Colchicine 0.6 mg Tablets and Mixed Amphetamine Salts 5 mg Extended Release Capsules, as well as clean the associated process equipment.

OBSERVATION 5

Investigations of an unexplained discrepancy and a failure of a batch or any of its components to meet any of its specifications did not extend to other batches of the same drug product.

Specifically,

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A.IR 21-071 "Major" incident occurred on 6/21/2021, because Potassium Chloride ER 750 mg Tablet (Lot GPC210378) material sticking to logo-side of punches which caused compression to be stopped. This was a repeat incident (Lot GPC210297), and the root cause was determined to be improper cleaning of (b) (4) punches after the previous batch was completed. The corrective action was rejection of tablets that did not meet weight and interactive training given to the two employees. The next batch (Lot GPC210379) was released and the investigation did not extend to other batches or associated discrepancies.

B.IR 22-002 "Major" incident occurred on 1/5/2022, and resulted in CAPA 22-007 initiated on 2/3/2022 to "Revise SOP MM-002 Rev 05 to 06 by clarifying the instructions on (b) (4) cleaning required when dispensing the excipients between batches of different products." However, the Potassium Chloride ER 750 mg tablets were released for use into next stage on 2/4/2022 because it was determined on 2/3/2022: "There is no impact on the materials since no API or color was used." Investigation did not extend to other batches or associated discrepancies and training of the employees was given on 1/11/2022, before the decision to revise the SOP was made on 2/3/2022.

C.IR 22-013 "Major" incident occurred on 1/24/2022 because a plastic window of the (b) (4) fell down into the (b) (4) Tablet Press GP-1102. The possible root cause was determined to be (b) (4) " As a result, (b) (4) tablets were retested with only one rejection as well as "Awareness" training provided to (b) (4) employees on the equipment SOP. The remainder of the batch was processed and released. The investigation did not extend to other batches or associated discrepancies.

OBSERVATION 6

There is a lack of written procedures describing in sufficient detail the methods, equipment and materials to be used for sanitation.

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Specifically,

A. Root cause of IR 22-002, was that employees (b) (6) and (b) (6) did not follow SOP MM-002-05 to perform (b) (4) cleaning in Room 129 because of a changeover to a different product excipient. However, as per CAPA 22-007 initiated on 2/3/2022, the SOP lacked sufficient detail for which cleaning method the employees were expected to follow as reflected by the statement in the CAPA, "Revise SOP MM-002 Rev 05 to Rev 06 by clarifying the instructions on (b) (4) cleaning required when dispensing the excipients between batches of different products." Also, the 1/11/2022 Training Form for the employees reflects "Awareness" training on SOP MM-002-05, and not version -06.

B. SOP GPM-077-01 effective 12/10/2021, entitled "Set-up, Operation and Cleaning of (b) (4) (b) (4) Capsule Filling Machine" (b) (4) cleaning ((b) (4)) beginning section 5.12, lacks sufficient detail for the cleaning with lint free wipes dampened with (b) (4) (b) (4).

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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."