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 ORAPHARMInternational483responses@fda.hhs.gov	02/14/2022-02/25/2022
	FEI NUMBER 3009083745

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Soumya Kumar Panda, Associate Vice President and Site Head

FIRM NAME	STREET ADDRESS
Mankind Pharma Limited	Block B & C, Opposite Dental College
CITY, STATE, ZIP CODE, COUNTRY Rampur Ghat, Himachal Pradesh, 173025, India	TYPE ESTABLISHMENT INSPECTED Drug Product 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 WE OBSERVED:

OBSERVATION 1

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,

1. Your firm's operation qualification (OQ) of the filter integrity test (FIT) machines is inadequate such that the filters, filter housings, and operating ranges (such as (b) (4) , flow rate etc.) associated with your drug products manufacturing were not part of the qualification. The OQ were conducted by the vendor on January 9, 2018 and completed on January 12, 2018 and only witnessed by your production and reviewed by quality assurance department. Your Senior General Manger of Quality Assurance and General Manager Production Block (b) were unable to explain the OQ document, specifically Operation Qualification Part 2 Instrument Part No. FFSO4 Serial No. 20295444. You attempted to qualify the FIT equipment for (b) (4) without use of any filter assembly. Your OQ document suggested that the FIT machine (Serial No. 20295444, ID # PID/C/087) was calibrated/qualified for (b) (4) with the help of a (b) (4) device at a preset value of (b) (4) . However, the specifications for several (b) (4) product filters at the (b) (4) stage include the (b) (4) FIT value of ≥(b) (4) mbar, outside of the calibrated/qualified range of ≥(b) (4) mbar. The firm failed to provide assurance that (b) (4) integrity testing of finished product is adequate to ensure sterility

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Rajiv R. Srivastava -S Digitally signed by Rajiv R. Srivastava -S DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2002112232, cn=Rajiv R. Srivastava -S Date: 2022.02.25 16:54:07 +05'30'	Rajiv Srivastava, CSO Dipesh Shah, CSO	02/25/2022

assurance. Some of such selected product filters associated with US products are listed in **Table 1**.

Table 1. Selected (b) (4) FIT for Product Filters Outside of the Qualification Range

Entry	Date	Time	Filtration Type	Filtration Stage	Filter Serial No.	Product Batch	(b) (4) (mbar) Spec.	(mbar) Result
1	7/14/2019	(b) (4)			8320	(b) (4)	≥(b) (4)	(b) (4)
2	7/21/2019				7301		≥(b) (4)	(b) (4)
3	1/8/2022				7441		≥(b) (4)	(b) (4)
4	1/29/2022				7234		≥(b) (4)	(b) (4)
5	10/29/220				1199		≥(b) (4)	(b) (4)
6	11/3/2020				2188		≥(b) (4)	(b) (4)

2. On February 16, 2022, we observed that your firm has more than ten (10) failed, aborted and / or error results recorded on the Filter Integrity Test (FIT) machine ID # PID/C/087 (Serial No. 20295444). The firm uses a total of (b) (4) FIT units (ID # (b) (4) (b) (4)) in the Manufacturing Block (b) . These FIT equipment are used to test filters which include: (b) (4) filter (to filter bulk drug products in Grade B), (b) (4) filters (to filter drug products in the filling line), disinfectant, (b) (4) and other items.

   Your Senior General Manager of Quality Assurance stated that a filter for (b) (4) stage can fail (b) (4) times and on the (b) (4) failure the filter is considered as failed. But the filter for (b) (4) (b) (4) can fail up to (b) (4) time and on (b) (4) failure the filter is considered as failed. This filter pass/fail criteria are addressed in SOP No. PID-017-07 (Effective date 8/9/2021) Procedure for Operation of Integrity Tester.

   Your Senior General Manager of Quality Assurance (Sr. GM QA) stated that the firm has not carried out the performance qualification (PQ) for the (b) (4) FIT machines in the Manufacturing Block (b) . The Sr. GM of QA also confirmed that retesting the product filters up to (b) (4) times was not qualified/verified/validated with respect to the drug product quality.

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov	02/14/2022-02/25/2022 FEI NUMBER 3009083745

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Soumya Kumar Panda, Associate Vice President and Site Head

FIRM NAME	STREET ADDRESS
Mankind Pharma Limited	Block B & C, Opposite Dental College
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Rampur Ghat, Himachal Pradesh, 173025, India	Drug Product Manufacturer

On February 16, 2022, we were provided with a list of failed /aborted /error FIT results for 2019 - 2021. Some of the selected multiple failed FIT results related to US market are included in **Table 2**.

Table 2. Selected Failed FIT Results for Drug Products Intended for the US Market:

Entry	Date	Time	Instrument ID	Area / Line	Filtration Type*	Filter Serial No.	Product Batch No.	Filter Integrity Test
1	1/24/2021	(b) (4)	PID/C/087	Vial	(b) (4)	8317	(b) (4)	
2	1/25/2021		PID/C/087	Vial		8317		
3	1/29/2021		PID/C/087	Vial		8315		
4	3/19/2021		PID/C/087	Vial		1188		
5	3/19/2021		PID/C/087	Vial		1188		
6	3/19/2021		PID/C/087	Vial		1188		
7	3/22/2021		PID/C/087	Vial		2061		
8	3/24/2021		PID/C/087	Vial		2138		
9	4/2/2021		PID/C/087	Vial		2159		
10	4/7/2021		PID/C/087	Vial		2124		
11	5/12/2021		PID/C/087	Vial		2103		
12	5/12/2021		PID/C/087	Vial		1196		
13	5/17/2021		PID/C/087	Vial		1182		
14	5/24/2021		PID/C/087	Vial		2132		
15	6/19/2021		PID/C/087	Vial		2266		
16	6/19/2021		PID/C/087	Vial		2266		
17	12/8/2020		PID/C/024	(b) (4)		1113		
19	9/29/2020		PID/C/056	(b) (4)		2114		

*(b) (4) filtration is for the filtration of bulk drug products in Grade B. (b) (4) filtration is for the filtration in the filling line in Grade A.

We also noted that you passed at least one of the (b) (4) product filters at the (b) (4) stage at a lower (b) (4) pressure ((b) (4) mbar) compared to the specification (Specification (b) (4) limit ≥

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Rajiv R. Srivastava -S Digitally signed by Rajiv R. Srivastava -S DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2002112232, cn=Rajiv R. Srivastava -S Date: 2022.02.25 16:57:40 +05'30'	Rajiv Srivastava, CSO Dipesh Shah, CSO	02/25/2022

(b) (4) mbar **Table 3**, Entry 4). Your Senior General Manager of Quality Assurance stated, after the filter failed for the (b) (4) time (**Table 3**, Entries 1-3), the firm used a (b) (4) of (b) (4) as the (b) (4) and recorded (b) (4) to pass the (b) (4) integrity product filter at a lower (b) (4) (**Table 3**, Entry 4). Your Senior General Manager of Quality Assurance stated that routine (b) (4) FIT at the (b) (4) is carried out with the product as the (b) (4). However, if the product is not available, in such case a (b) (4) of (b) (4) is used as the (b) (4). We also observed use of low surface tension fluid as (b) (4) (after third failure of the (b) (4)) in your procedure, SOP No. PID-017-07 (page 57, Effective date 8/9/2021) Procedure for Operation of Integrity Tester.

As per the Operation Qualification Part 2 for FIT Machine Serial No. 20295444 (ID # PID/C/087), you have attempted to qualify this FIT machine at (b) (4) mbar. Hence the recorded (b) (4) mbar is outside the equipment qualification range.

Table 3. FIT Test Result for Batch No. (b) (4) on FIT Machine PID/C/087

Entry	Date	Time	Filtration Type	Filter Sr. No	Result	(b) (4) (mbar) Spec.	(b) (4) (mbar) Observed
1	3/19/2021	(b) (4)		1188	Fail	≥ (b) (4)	(b) (4)
2	3/19/2021			1188	Fail	≥ (b) (4)	
3	3/19/2021			1188	Fail	≥	
4	3/19/2021			1188	Pass	≥	

OBSERVATION 2

Equipment and utensils are not cleaned and sanitized at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product.

Specifically,

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov	02/14/2022-02/25/2022
	FEI NUMBER 3009083745

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Soumya Kumar Panda, Associate Vice President and Site Head

FIRM NAME	STREET ADDRESS
Mankind Pharma Limited	Block B & C, Opposite Dental College
CITY, STATE, ZIP CODE, COUNTRY Rampur Ghat, Himachal Pradesh, 173025, India	TYPE ESTABLISHMENT INSPECTED Drug Product Manufacturer

1. On February 14, 16 and 22, 2022, residue was witnessed on the inside surface of the (b) (4) (b) (4) which are directly connected to your (b) (4) and (b) (4) machines. You utilize (b) (4) non-dedicated (b) (4) and (b) (4) non-dedicated (b) (4) machines to manufacture products that are shipped to the US.

   a. On February 14, 2022, the (b) (4) liters (Equipment ID: PT/AC/005) located in (b) (4) area of manufacturing Block (b) was opened and was observed to contain, a layer of white powder what appears to be drug product residue on the inside surface of the (b) (4).

   According to Deputy Manager Production, the firm uses Standard Operating Procedure (SOP), PTD-059-04, document titled, 'Cleaning and Operation of (b) (4) Litre' with effective date of July 20, 2020 to clean the (b) (4). However, this SOP does not include procedures to clean the inside surface of the (b) (4). He further stated that the inside surface of the (b) (4) are cleaned using (b) (4) washing system ((b) (4) System).

   Since February 2020 (b) (4): Equipment ID: PT/AC/005 is used to manufacture the following commercial products

S. No.	Products Manufactured (February 1, 2020 to February 18, 2022)	Quality Shipped to US (In (b) (4))
1	(b) (4) Capsules USP	(b) (4)
2	(b) (4) Tablets USP	(b) (4)
	Total	(b) (4)

The following exhibit batches were also manufactured in the (b) (4), since February 2020 in (b) (4)

S. No.	Exhibit Batches Manufactured (February 1, 2020 to February 18, 2022)	Quality (In (b) (4))

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Rajiv R. Srivastava -S Digitally signed by Rajiv R. Srivastava -S DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2002112232, cn=Rajiv R. Srivastava -S Date: 2022.02.25 16:59:22 +05'30'	Rajiv Srivastava, CSO Dipesh Shah, CSO	02/25/2022

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov	02/14/2022-02/25/2022
	FEI NUMBER 3009083745

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Soumya Kumar Panda, Associate Vice President and Site Head

FIRM NAME	STREET ADDRESS
Mankind Pharma Limited	Block B & C, Opposite Dental College
CITY, STATE, ZIP CODE, COUNTRY Rampur Ghat, Himachal Pradesh, 173025, India	TYPE ESTABLISHMENT INSPECTED Drug Product Manufacturer

1	(b) (4) Tablets		(b) (4)
2	(b) (4) Tablets USP		
3	(b) (4) Tablets USP		
4	(b) (4) Tablets USP		
5	(b) (4) Tablets USP		
6	(b) (4) Tablets USP		
7	(b) (4) Capsules		
8	(b) (4) Capsules USP		
9	(b) (4) Caps USP		
10	(b) (4) Capsules USP		
	Total		

b. On February 14, 2022, the (b) (4) liters (Equipment ID: PT/AC/014) located in (b) (4) (b) area of manufacturing Block (b) (4) was opened and was observed to contain a layer of white powder what appears to be drug product residue on the inside surface of the (b) (4).

According to Deputy Manager Production, the firm uses Standard Operating Procedure (SOP), PTD-058-06, document titled, 'Cleaning and Operation of (b) (4) Litre' with effective date of January 13, 2022 to clean the (b) (4). However, this SOP does not include procedures to clean the inside surface of the (b) (4). He further stated that the inside surface of the (b) (4) are cleaned using (b) (4) washing system ((b) (4) System).

Since February 2020 (b) (4): Equipment ID: PT/AC/014 is used to manufacture the following products

The following exhibit batches were also manufactured in the (b) (4), since February 2020

S. No.	Exhibit Batches Manufactured (February 1, 2020 to February 18, 2022)	Quality (In (b) (4))

SEE REVERSE OF THIS PAGE

EMPLOYEE(S) SIGNATURE
Rajiv R. Srivastava -S
Digitally signed by Rajiv R. Srivastava -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2002112232, cn=Rajiv R. Srivastava -S
Date: 2022.02.25 17:00:11 +05'30'

EMPLOYEE(S) NAME AND TITLE (Print or Type)
Rajiv Srivastava, CSO
Dipesh Shah, CSO

DATE ISSUED
02/25/2022

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov	02/14/2022-02/25/2022
	FEI NUMBER 3009083745

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Soumya Kumar Panda, Associate Vice President and Site Head

FIRM NAME	STREET ADDRESS
Mankind Pharma Limited	Block B & C, Opposite Dental College
CITY, STATE, ZIP CODE, COUNTRY Rampur Ghat, Himachal Pradesh, 173025, India	TYPE ESTABLISHMENT INSPECTED Drug Product Manufacturer

1	(b) (4) Tabs USP		(b) (4)
2	(b) (4)		
3	(b) (4) Tablets		
4	(b) (4) Tablets USP		
	Total		

c. On February 16, 2022, the (b) (4) liters (Equipment ID: PTD/B/205) located in (b) (4) (b) (4) area of manufacturing Block (b) was opened and was observed to contain a layer of white powder what appears to be drug product residue on the inside surface of the (b) (4).

According to Deputy Manager Production, the firm uses Standard Operating Procedure (SOP), PTD-132-03, document titled, 'Cleaning and Operation of (b) (4) Litre' ((b) (4))' with effective date of January 7, 2022 to clean the (b) (4). However, this SOP does not include procedures to clean the inside surface of the (b) (4). He further stated that the inside surface of the (b) (4) are cleaned using (b) (4) washing system ((b) (4) System).

Since February 2020 (b) (4): Equipment ID: PTD/B/205 is used to manufacture the following products

S. No.	Products Manufactured (February 1, 2020 to February 18, 2022)	Quality Shipped to US (In (b) (4))
1	(b) (4) Tablets USP	(b) (4)
	Total	(b) (4)

The following exhibit batches were also manufactured in the (b) (4), since February 2020

S. No.	Exhibit Batches Manufactured (February 1, 2020 to February 18, 2022)	Quality (In (b) (4))

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Rajiv R. Srivastava -S Digitally signed by Rajiv R. Srivastava -S DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2002112232, cn=Rajiv R. Srivastava -S Date: 2022.02.25 17:01:06 +05'30'	Rajiv Srivastava, CSO Dipesh Shah, CSO	02/25/2022

1	(b) (4) Capsules USP		(b) (4)
2	(b) (4) Capsule		(b) (4)
	Total		(b) (4)

d. On February 14, 2022, the (b) (4) liters (Equipment ID: PT/AC/144) located in (b) (4) area of manufacturing Block (b) was opened and was observed to contain a layer of white powder what appears to be drug product residue on the inside surface of (b) (4).

According to Deputy Manager Production, the firm uses Standard Operating Procedure (SOP), PTD-129-03, document titled, 'Cleaning and Operation of (b) (4) Litre' with effective date of December 17, 2021 to clean the (b) (4). However, this SOP does not include procedures to clean the inside surface of the (b) (4). He further stated that the inside surface of the (b) (4) are cleaned using (b) (4) washing system ((b) (4) System).

Since February 2020 (b) (4): Equipment ID: PT/AC/144 is used to manufacture the following products

S. No.	Products Manufactured (February 1, 2020 to February 18, 2022)	Quality Shipped to US (In (b) (4))
1	(b) (4) Tablet USP	(b) (4)
	Total	(b) (4)

The following exhibit batches were also manufactured in the (b) (4), since February 2020

S. No.	Exhibit Batches Manufactured (February 1, 2020 to February 18, 2022)	Quality (In (b) (4))
1	(b) (4) Tablets USP	(b) (4)
2	(b) (4) Tabs USP	(b) (4)

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov	02/14/2022-02/25/2022
	FEI NUMBER 3009083745

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Soumya Kumar Panda, Associate Vice President and Site Head

FIRM NAME	STREET ADDRESS
Mankind Pharma Limited	Block B & C, Opposite Dental College
CITY, STATE, ZIP CODE, COUNTRY Rampur Ghat, Himachal Pradesh, 173025, India	TYPE ESTABLISHMENT INSPECTED Drug Product Manufacturer

3	(b) (4) Tablets USP		(b) (4)
4	(b) (4) Tablets		
5	(b) (4) Capsules		
6	(b) (4) Capsules USP		
	Total		

e. On February 14, 2022, the (b) (4) liters (Equipment ID: PTD/B/300) located in (b) (4) area of manufacturing Block (b) was observed to contain layer of white powder what appears to be drug product residue was seen on the inside surface of (b) (4).

According to Deputy Manager Production, the firm uses Standard Operating Procedure (SOP), PTD-169-01, document titled, 'Cleaning and Operation of (b) (4) Equipment (b) (4) C' with effective date of January 21, 2021 to clean the (b) (4). However, this SOP does not include procedures to clean the inside surface of the (b) (4). He further stated that the inside surface of the (b) (4) are cleaned using (b) (4) washing system ((b) (4) System).

Since February 2020 (b) (4): Equipment ID: PTD/B/300 is used to manufacture the following exhibit batches.

S. No.	Exhibit Batches Manufactured (February 1, 2020 to February 18, 2022)	Quality (In (b) (4))	
1	(b) (4) Caps USP		(b) (4)
2	(b) (4) Capsule		(b) (4)
	Total		(b) (4)

f. On February 22, 2022, (b) (4) (Equipment ID: PT/AC/058) located in (b) (4) area of manufacturing Block (b) was observed to contain (b) (4) and (b) (4) residue on the inside surface of the (b) (4).

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Rajiv R. Srivastava -S Digitally signed by Rajiv R. Srivastava -S DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2002112232, cn=Rajiv R. Srivastava -S Date: 2022.02.25 17:03:05 +05'30'	Rajiv Srivastava, CSO Dipesh Shah, CSO	02/25/2022

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov	02/14/2022-02/25/2022
	FEI NUMBER 3009083745

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Soumya Kumar Panda, Associate Vice President and Site Head

FIRM NAME	STREET ADDRESS
Mankind Pharma Limited	Block B & C, Opposite Dental College
CITY, STATE, ZIP CODE, COUNTRY Rampur Ghat, Himachal Pradesh, 173025, India	TYPE ESTABLISHMENT INSPECTED Drug Product Manufacturer

According to Deputy Manager Production, the firm uses Standard Operating Procedure (SOP), PTD-071-05, document titled, 'Cleaning and Operation of (b) (4) with effective date of November 11, 2021 to clean the (b) (4). However, this SOP does not include procedures to clean the inside surface of the (b) (4).

Since February 2020 (b) (4): Equipment ID: PT/AC/058 is used to manufacture the following products

S. No.	Products Manufactured (February 1, 2020 to February 18, 2022)		Quality Shipped to US (In (b) (4))
1	(b) (4)	Tablets USP (b) (4) mg	(b) (4)
2	(b) (4)	Tablets USP (b) (4) mg	
3	(b) (4)	Tablets USP (b) (4) mg	
4	(b) (4)	Tablets USP (b) (4) mg	
5	(b) (4)	Tablets USP (b) (4) mg	
		Total	

The following exhibit batches were also manufactured in the (b) (4), since February 2020

S. No.	Exhibit Batches Manufactured (February 1, 2020 to February 18, 2022)		Quality (In (b) (4))
1	(b) (4)	Tablets USP (b) (4) mg	(b) (4)
		Total	(b) (4)

g. On February 22, 2022, (b) (4) (Equipment ID: PT/AC/056) located in (b) (4) area of manufacturing Block (b) was observed to contain white residue on the inside surface of the (b) (4).

According to Deputy Manager Production, the firm uses Standard Operating Procedure (SOP),

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Rajiv R. Srivastava -S Digitally signed by Rajiv R. Srivastava -S DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2002112232, cn=Rajiv R. Srivastava -S Date: 2022.02.25 17:04:14 +05'30'	Rajiv Srivastava, CSO Dipesh Shah, CSO	02/25/2022

PTD-072-04, document titled, 'Cleaning and Operation of (b) (4) with effective date of November 12, 2021 to clean the (b) (4). However, this SOP does not include procedures to clean the inside surface of the (b) (4).

Since February 2020 (b) (4): Equipment ID: PT/AC/056 is used to manufacture the following products

S. No.	Products Manufactured (February 1, 2020 to February 18, 2022)	Quality Shipped to US (In (b) (4))
1	(b) (4) Tablets USP (b) (4) mg	(b) (4)
2	(b) (4) Tablets USP (b) (4) mg	
3	(b) (4) Tablets USP (b) (4) mg	
4	(b) (4) Tablets USP (b) (4) mg	
5	(b) (4) Tablets USP (b) (4) mg	
6	(b) (4) Tablets USP (b) (4) mg	
	Total	

The following exhibit batches were also manufactured in the (b) (4), since February 2020

S. No.	Exhibit Batches Manufactured (February 1, 2020 to February 18, 2022)	Quality (In (b) (4))
1	(b) (4) mg + (b) (4) mg Tablets	(b) (4)
	Total	(b) (4)

h. On February 22, 2022, (b) (4) (Equipment ID: PT/AC/147) located in (b) (4) area of manufacturing Block (b) was observed to contain, (b) (4) residue on the (b) (4) and (b) (4) and (b) (4) residue on the inside surface of the (b) (4).

According to Deputy Manager Production, the firm uses Standard Operating Procedure (SOP),

PTD-119-06, document titled, 'Cleaning and Operation of (b) (4) with effective date of January 21, 2022 to clean the (b) (4). However, this SOP does not include procedures to clean the inside surface of the (b) (4).

Since February 2020 (b) (4): Equipment ID: PT/AC/147 is used to manufacture the following products

S. No.	Products Manufactured (February 1, 2020 to February 18, 2022)	Quality Shipped to US (In (b) (4))
1	(b) (4) Tablets USP (b) (4) mg	(b) (4)
2	(b) (4) Tablets USP (b) mg	
3	(b) (4) Tablets USP (b) (4) mg	
4	(b) (4) Tablets USP (b) (4) mg	
	Total	

The following exhibit batches were also manufactured in the (b) (4), since February 2020

S. No.	Exhibit Batches Manufactured (February 1, 2020 to February 18, 2022)	Quality (In (b) (4))
1	10 different types of products with different strengths for a total of 26 strengths and types of products	(b) (4)
	Total	(b) (4)

During the inspection, I was provided with schematic diagrams for PT/AC/058, PT/AC/056 and PTD/AC/147 (b) (4).

2. On February 14 and 16, 2022, a total of eleven (11) samples of the white powder residue were

taken from non-dedicated (b) (4). Your firm tested each sample relative to the history of the products run on their respective (b) (4) and your Quality Control Department could not identify the white powder residue which included the last product run on the respective (b) (4).

a. PT/AC/005 located in (b) (4) area the last product run was (b) (4) tablets USP (b) (4) mg ((b) (4)) (Batch # (b) (4)) on which was run on January 4, 2022. The sample analysis results are Not Detected.
b. PT/AC/014 located in (b) (4) area the last product run was (b) (4) tablets USP (b) (4) / (b) (4) mg ((b) (4)) (Batch # (b) (4)) which was run on February 12, 2022. The sample analysis results are Not Detected.
c. PTD/B/205 located in (b) (4) area the last product run was (b) (4) tablets USP (b) (4) / (b) (4) mg ((b) (4)) (Batch # (b) (4)) which was run on February 15, 2022. The sample analysis ((b) (4) samples taken on February 16, 2022) results are Not Detected and Below Quantitative limit
d. PTD/B/300 located in (b) (4) area the last product run was (b) (4) Capsules USP (b) (4) mg (Batch # (b) (4)) which was run on August 23, 2021. The sample analysis results are Not Detected.
PT/AC/144 located in (b) (4) area the last product run was (b) (4) tablets USP (b) (4) mg ((b) (4)) (Batch # (b) (4)) which was run on January 1, 2022. The sample analysis results are Not Detected.

3. Scratches, dents, and (b) (4) color material deposition was observed on your (b) (4) mm (b) (4) stopper transfer (b) (4) bowl. This (b) (4) Bowl did not have any identification but did have an inscription that read in part ***20190918101*** on the front side of the (b) (4) Bowl. According to your Production Manager, the (b) (4) Bowl was used for the manufacturing of Batch No. (b) (4). Your Production Manager also stated this (b) (4) Bowl was cleaned; after use with WFI and sterilized. The (b) (4) material deposition on the (b) (4) mm (b) (4) Bowl (read in part ***20190918101***) was confirmed by wiping the dirty surface of this (b) (4) Bowl with a white lint free cloth. The portion of the lint free cloth that was rubbed against the (b) (4) surface of the (b) (4) Bowl revealed (b) (4) and (b) (4) spots. You have at least particulate matter related OOS results including OOS-21-PU3C-

IP-001 for drug product Batch No (b) (4) that was filled on the vial filling line where the (b) (4) mm (b) (4) Bowl (read in part ***20190918101***) was used.

OBSERVATION 3

Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the room to produce aseptic conditions.

Specifically,

1. (b) (4) screens that cover the HEPA filter are not cleaned and sanitized during pre and post manufacturing in the Vial Filling and Stoppering Machine ID # PID/C/067. These (b) (4) screens are used to aid homogeneous diffusion of the air from HEPA into the (b) (4) grade A filling area. Your procedure SOP No. PID-008-11 (Effective date 11/24/2021), Cleaning and Sanitization of Aseptic Area, does not have a provision to clean and sanitize the (b) (4) screens. Your procedure SOP No. PID-076-09 (Effective date 1/11/2022), Operation and Cleaning of Vial Filling and Stoppering Machine does not have provision for sanitizing the (b) (4) screen. As per your SOP No. PID-065-03 (Effective date 2/10/2021) Operation and Cleaning of (b) (4), you carry out (b) (4) of clean area (including filling room) (b) (4) days but there is no instruction for cleaning/sanitization for the (b) (4) screen post (b) (4). You use (b) (4) as a (b) (4) disinfectant.

   Your Senior Executive, Production stated that the (b) (4) screens are replaced (b) (4) and cleaned during the initial installation as per your SOP No. PID-003-10 (Effective date 12/24/2021, page 27) Material Movement.

2. The (b) (4) effectiveness study has not been carried out for the Block (b) (4) manufacturing area where sterile drugs are manufactured. As per your procedure SOP No. PID-065-03 (Effective date 2/10/2021) Operation and Cleaning of (b) (4), you carry out (b) (4) of clean area (including filling room) (b) (4). Your Senior Manager for Production Block (b) shared a document for

the (b) (4) study for Block (b), Document No. PU3C-MIS-001-00 (Effective date 4/19/2018) Miscellaneous Protocols Cum Report for Assessment of (b) (4) Time of (b) (4) in Clean Area of Block (b). This document only has an assessment of time that the (b) (4) took to (visually) cover the entire area of the room with (b) (4) (the (b) (4) disinfectant). However, you have no data to verify the effectiveness of the (b) (4). In addition, you have not established the (b) (4) phase times for the (b) (4). Hence, there is no assurance that the drug products are manufactured in an aseptic conditions/environment. Additionally, you failed to provide assurance that (b) (4) does not cross contaminate your aseptically filled products.

OBSERVATION 4

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

Specifically,

1. Your current filling equipment design fails to assure that grade A environment is maintained on your infeed (b) (4). You use an approximately (b) (4) diameter Infeed (b) (4) to feed the vials (coming out of the Vial (b) (4) ID # PID/C/066) to the filling station. The nearest station for (b) (4) viable and (b) (4) non-viable particle monitoring location is about (b) (4) away from the edge of (~ (b) (4) diameter) Infeed (b) (4). Therefore, there is no assurance the vials on Infeed (b) (4) are maintained under grade A.

2. NVPC are not recorded for the Vial Capping Machine ID # PID/C/068. The drug product filled, and (b) (4) stoppered vials are sealed on Vial Capping Machine ID # PID/C/068 that is approximately (b) (4) (from the filling station) in a RABS in grade C Sealing Room (b) (4). During the drug product manufacturing, you carry out the environmental monitoring of the Vial Filling and Stoppering Machine ID # PID/C/067 with (b) (4) NVPC including: IDs (b) (4). The nearest NVPC to the Vial Capping Machine ID # PID/C/068 is NVPC ID # PID/C/216 that is almost (b) (4) away near the Vial (b) (4) zone. Hence there is no

assurance that Vial Capping Machine ID # PID/C/068 is maintained under grade A. In addition, you have recorded at least one deviation (# DEV-PA-007-21-0010) where an unstopped vial was found amongst the sealed vials suggesting that (b) (4) stoppers may not be fully seated (or missing) before reaching the Vial Capping Machine ID # PID/C/068.

3. You do not record NVPC for the Mobile LAFUs while transferring the sterilized equipment and materials from (b) (4) to the filling lines. You have (b) (4) Mobile LAFUs in Vial Filling and Stoppering Machine Room grade B area (IDs # (b) (4)) and (b) (4) in the (b) (4) (b) (4) Machine Room Grade C area (ID # (b) (4)). You record (b) (4) NVPC data as per SOP No. PID-102-05 (Effective date 5/25/2021) Monitoring of Non-Viable Particle Count by Portable Particle Counter in Vial Line. There is no instruction as to when the data should be taken; before, during, or after the use of Mobile LAFUs. Your Senior Executive from Production stated that he takes (b) (4) NVPC data for Mobile LAFUs ID # (b) (4) prior to the use (operation) of Mobile LAFUs on the day of manufacturing. Therefore, there is no assurance that the inside of the Mobile LAFUs is maintained under grade A when sterilized equipment and materials are transferred from (b) (4) to the filling lines.

4. Your airflow visualization studies conducted for (b) (4) machine (ID # PID/C/034) are inadequate to demonstrate unidirectional air flow under dynamic conditions. The (b) (4) machine is kept in Filling Room (b) (4) in grade C area. The only smoke study you carried out for the (b) (4) machine is at the static condition and just about (b) (4) long. There is not enough smoke to verify the sweeping of filling zone and the surrounding grade C area to establish grade A zone in the direct vicinity of the filling zone. In addition, you failed to demonstrate adequate particulate control during dynamic operations. The only data to verify a Grade A in the filling zone is the active air sampling, that to (b) (4) in an (b) (4) . However, the location for active air sampling (ID # FAS015) is closer to the filling (b) (4) in the resting position. During the filling operation the filling (b) (4) travels (b) (4) into the (b) (4) in the grade C area. The discharge of drug product into the (b) (4) takes place in the grade C. Your smoke study in the static condition do not verify sweeping of the grade C filling zone to be a grade A area.

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov	02/14/2022-02/25/2022
	FEI NUMBER 3009083745

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Soumya Kumar Panda, Associate Vice President and Site Head

FIRM NAME	STREET ADDRESS
Mankind Pharma Limited	Block B & C, Opposite Dental College
CITY, STATE, ZIP CODE, COUNTRY Rampur Ghat, Himachal Pradesh, 173025, India	TYPE ESTABLISHMENT INSPECTED Drug Product Manufacturer

OBSERVATION 5

There is a failure to thoroughly review any unexplained discrepancy whether or not the batch has already been distributed.

Specially,

1. Your investigation for Deviation No. DEV-PA-007-21-0010 is inadequate such that you did not investigate all the contributing factors. The deviation was initiated because of finding a sealed vial (with (b) (4) flip cap) with the missing (b) (4) stopper (a critical defect) amongst the sealed vials of Batch No. (b) (4) . No picture of the vial with the missing (b) (4) stopper was available for the investigation. You did not investigate the Vial Filling and Stoppering Machine ID # PID/C/067 to verify whether or not a (b) (4) stopper was actually seated on the vial before the vial moved out from the Vial (b) (4) zone and made its way into the Vial Capping Machine ID # PID/C/068. In addition, the investigation of the Vial Capping Machine ID # PID/C/068 did not include challenging the sensors with defects at the speed that is similar to the vial filling and sealing speed.

2. During the inspection, while reviewing Out of Specification (OOS) I observed four OOS's OOS-20-PU3C-SS-012 dated December 30, 2020; OOS-20-PU3C-SS-010 dated October 3, 2020, OOS-21-PU3C-IP-012 dated June 11, 2021 and OOS-21-PU3C-IP-016: August 26, 2021 where your firm inadequately conducted and documented analysist interview during OOS Phase I investigations. While interviewing Executive Quality Control employee who interviews analyst during OOS investigations stated that he interviews analyst by the use of form GSOP-009/F2-03. He stated that the interview is conducted in front of his pears and asking the analyst only the questions on the document.

   In addition, I interviewed the analyst who was interviewed during the OOS-21-PU3C-IP-016 investigation (page 28 of the OOS) stated that the interview indeed took place at his workstation in front of his peers. He added that the interview was structured and only provided answers to the

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Rajiv R. Srivastava -S Digitally signed by Rajiv R. Srivastava -S DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2002112232, cn=Rajiv R. Srivastava -S Date: 2022.02.25 17:14:06 +05'30'	Rajiv Srivastava, CSO Dipesh Shah, CSO	02/25/2022

questions on the check list; no extra information was given by him.

At the end of Executive Quality Control employee interview, he stated all interviews are conducted in the same manor.

OBSERVATION 6

There are no written procedures for production and process controls designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess.

Specifically, your firm's process of cleaning the (b) (4) by way of a (b) (4) washing system ((b) (4) System) is inadequate. This system uses a jet spray that are located in the (b) (4) part of the (b) (4) which lead directly into the (b) (4). According to Deputy Manager Production and page 3, section 5.0 of SOP, SOP-PA-PTD-085, 1.0, document titled, 'Cleaning and Operation of (b) (4) Washing System ((b) (4) System)' with effective date February 5, 2022, these sprayers are used between (b) (4) and (b) (4) same manufactured product batch. Your firm qualified these sprayers according to protocol number PU3B-MIS-093-01 with approved date February 3, 2022. The cleaning of the (b) (4) is inadequate because product residue was observed.