DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parkland Drive, Room 2093 Rockville, MD 20857 Industry Information: www.fda.gov/oc/industry	09 June 2022 to 20 June 2022* FEI NUMBER 3014210753

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Viral Shah, Managing Director

FIRM NAME	STREET ADDRESS
Immacule Lifesciences Private Ltd. India	Village Thanthewal, Ropar Road
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Nalagarh, District Solan, Himachal Pradesh 174 101	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) (WE) OBSERVED

OBSERVATION # 1

Equipment for adequate control over air pressure, humidity, and temperature is not provided when appropriate for the manufacture, processing, packing or holding of a drug product.

Specifically,

The consistent supply of positive differential pressure to the aseptic filling suite, including the vial and ampoule filling lines cannot be assured in the case of power failure or other factors. The firm has (b) (4) diesel generators and (b) (4) UPS (uninterruptible power supply) units in case of electrical power failure. The UPS provides power to critical equipment in case of failure of both electrical power and the diesel generators. The firm monitors actual pressure (not differential pressure) in manufacturing rooms and only the filling lines have differential pressure information. Continuous differential pressure readings are not available for the filling lines (vial and ampoule).

a) On 13 June 2021, electrical power and power from the diesel generators failed from (b) (4) to (b) (4) hours. The air handling units (AHU) stopped working in Block (b) (4) and Block (b) (4) impacting on the control of temperature, relative humidity, and air flow pressures in Production, Warehouse, Packing, Quality Control, and the Microbiology Laboratory.

i. Vial Filling Line set up was in progress for (b) (4) Batch # (b) (4) from (b) (4) to (b) (4) hours, when power failure occurred. The firm reports the LAF for the vial filling (b) (4) was continuously running on UPS backup power but was not able to provide differential pressure readings for this time period.

Add Continuation Page

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Cynthia Jim, CSO Wayne D. McGrath, CSO	06/20/2022

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parkland Drive, Room 2093 Rockville, MD 20857 Industry Information: www.fda.gov/oc/industry	09 June 2022 to 20 June 2022* FEI NUMBER 3014210753

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Viral Shah, Managing Director

FIRM NAME	STREET ADDRESS
Immaculé Lifesciences Private Ltd. India	Village Thanthewal, Ropar Road
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Nalagarh, District Solan, Himachal Pradesh 174 101	Manufacturer

ii. The firm reports no product impact for aseptic filling operations but the following excursions occurred: The vial sterile area exit change room had a pressure drop to 0.00 PA from set point of (b) (4) PA; the vial sterile are holding area had a pressure drop to 0.07 PA from set point of (b) (4) PA; the filling and stoppering area had a pressure drop to 0.09 PA from set point of (b) (4) PA; and the Sterile Area Entry change room had a pressure drop to 0.05 PA from set point of (b) (4) PA.

iii. No product impact was also concluded for all areas of the aseptic filling suite including grade A and B areas although pressure readings dropped below specifications. For example, the Compounding area had a pressure drop to 2.23 PA from set point of (b) (4) PA and the Sterile Area Entry change room pressure dropped to 0.05 PA from set point of (b) (4) PA.

b) On 24 September 2021, electrical power and power from the diesel generators failed from (b) (4) to (b) (4) hours. The air handling units (AHU) stopped working in Block (b) (4) and Block (b) (4)

i. Filling line set up had been initiated for (b) (4) Injection (b) (4) mg (b) (4) mL. batch # (b) (4) at (b) (4) when the power failed and AHU # 2 powering the vial filling line stopped working. The firm concluded no product impact although no differential pressure readings are available the (b) (4) vial filling line during the power failure.

ii. No product impact was also concluded for all areas of the aseptic filling suite including grades A and B area although pressure readings dropped below specification. For example, the male sterile gowning room dropped to 0.42 PA below set point of (b) (4) PA and Compound area dropped to 3.47 PA from set point of (b) (4) PA.

c) On 18 August 2021 and 19 August 2021, electrical power failure occurred. As a result, the AHUs for Blocks (b) (4) & (b) (4) stopped working for 9 minutes on 18 August 2021 and 5 minutes on 19 August 2021.

i. Filling line set up had been completed for (b) (4) njection / (b) (4) (b) (4) ng/vial Batch # (b) (4) during the nine minutes (19:15 to 19:24) of power failure on 18 August 2021 but

Add Continuation Page

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Cynthia Jim	Cynthia Jim, CSO Wayne D. McGrath, CSO	06/20/2022

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parkland Drive, Room 2093 Rockville, MD 20857 Industry Information: www.fda.gov/oc/industry	09 June 2022 to 20 June 2022* FEI NUMBER 3014210753

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Viral Shah, Managing Director

FIRM NAME	STREET ADDRESS
Immacule Lifesciences Private Ltd. India	Village Thanthewal, Ropar Road
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Nalagarh, District Solan, Himachal Pradesh 174 101	Manufacturer

filling had not started. The firm reports no product impact since the laminar air flow (LAF) for the vial filling line (b) (4) RABs) was powered by the UPS, but no differential pressure readings are available during the power failure.

ii. No product impact was also concluded for all areas of the aseptic filling suite including grades A and B although pressure readings dropped below specification. For example, the pressure in the Grade B corridor dropped to 2.75 from set point of (b) (4) PA and the pressure to Sterile Area Entry Change Room dropped to 0.02 PA from set point of (b) (4) PA.

iii. No product impact was concluded for power failure of five minutes on 19 August 2021 as no manufacturing activity was reported for the vial filling suite although pressure readings dropped below specification and relative humidity readings exceeded specifications.

OBSERVATION # 2

The written stability testing program is not followed.

Specifically,

a) Samples stored for stability testing are not always maintained at specified temperatures. Temperature excursions have occurred for stability chamber QA/COC-02 used for storing samples at 2-8°C. For example,

- 19 April 2020 – (b) (4) with highest temperature recorded of 23.6°C
- 13 July 2020 – (b) (4) with highest temperature recorded of 71.4°C
- 17 July 2020 – (b) (4) with highest temperature recorded of 22.5°C
- 29 July 2020 – (b) (4) with highest temperature recorded of 24.7°C
- 23 August 2020 – (b) (4) with highest temperature recorded of 27°C
- 20 August 2021 – (b) (4) with highest temperature recorded of 27°C
- 15 October 2021 – (b) (4) with highest temperature recorded of 28.3°C
- 08 November 2021 – (b) (4) with highest temperature recorded of 25.5°C.

Add Continuation Page

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Cynthia Jim	Cynthia Jim, CSO Wayne D. McGrath, CSO	06/20/2022

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parkland Drive, Room 2093 Rockville, MD 20857 Industry Information: www.fda.gov/oc/industry	09 June 2022 to 20 June 2022* FEI NUMBER 3014210753

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Viral Shah, Managing Director

FIRM NAME	STREET ADDRESS
Immacule Lifesciences Private Ltd. India	Village Thanthewal, Ropar Road
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Nalagarh, District Solan, Himachal Pradesh 174 101	Manufacturer

i. Temperature excursions were considered acceptable until the excursion reached (b) (4) SOP/QA/083 Stability Program Management, requires "the storage conditions and any alarms shall be monitored by QA Officer / Executive … short term spikes till a maximum of (b) (4) are acceptable". No action was taken for the four of eight above examples where temperature excursions lasted greater than (b) (4)

ii. There is no requirement to initiate an Incident/Investigation for temperature excursions, including excursions exceeding (b) (4) SOP/QA/083 Stability Program Management, requires "If the stability chamber is not rectified within (b) (4) the stability samples shall be shifted to back up chamber …". No incidents/investigations were initiated, and samples were not moved when temperature excursion exceeded (b) (4)

iii. Procedures do not include a requirement to evaluate samples for adverse impact as a result of temperatures exceeding specified limits. Eight of eight examples provided above exceeded 20C, yet action was not taken to evaluate the samples for adverse impact.

b) Storage of long-term stability samples outside specified temperatures of 2-8°C have adversely impacted testing of stability samples. For example,

i. OOS/21/027 was initiated 02 December 2021 when stability study analysis of (b) (4) injection USP (b) (4) ng/mL batches (b) (4) and (b) (4) were OOS for related substance. (b) (4) injection USP (b) (4) ng/mL batches (b) (4) and (b) (4) were released to the U.S. client on 30 September 2021 and 22 October 2021 respectively. Testing of additional samples obtained from the U.S. client in January 2022 were found complying to specifications. The additional samples obtained were used to replace the stability samples that had experienced temperature excursions.

ii. OOS/21/028 was initiated 26 December 2021 when stability samples (b) (4) Injection, USP (b) (4) ncg/mL batches (b) (4) and (b) (4) tested OOS for related substance and assay results at the 6 month stability timepoint. Significant decrease in assay results were observed at the 6 month timepoint. Retention samples were tested and found within specification. Samples experiencing temperature excursions were

Add Continuation Page

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Cynthia Jim, CSO Wayne D. McGrath, CSO	06/20/2022

replaced with retention samples that had been stored in the warehouse 2-8°C storage unit.

iii. OOS/22/003 was initiated 13 February 2022 when (b) (4) injection (b) (4) mg (b) mL batch # (b) (4) was found out of specification for Related Compound (b) (4) at the 18 month timepoint. The firm determined the OOS was related to the temperature excursion and replaced stability samples with retention samples that had been stored in the warehouse 2-8°°C chamber.

iv. The samples stored in stability chamber QA/COC-02 with evidence of temperature excursions have not been evaluated for product impact. For example, (b) (4) injection USP (b) (4) ng/mL exhibit batches # (b) (4) were OOS for related substances at the 24 month time point and (b) (4) njection USP (b) (4) ng/mL exhibit batches # (b) (4) (b) (4) were OOS at the 18 month timepoint. These OOSs were confirmed prior to temperature excursions in October and November 2021, but the lots were not evaluated for adverse impact from temperature excursions in the 2-8°C stability chamber in 2020.

OBSERVATION # 3
The responsibilities and procedures applicable to the quality control unit are not in writing.

Specifically,
Supervisory personnel and/or QA personnel did not assure the accuracy of reported test results. For example,

a) The accuracy of stability test results were not verified prior to approving test results for the 18 & 24 month Stability Summary Reports for (b) (4) USP (b) (4) mg/ml batch # (b) (4) The Stability Summary Reports were reviewed by Manager of QC and approved by Senior Manager of QA.

i. The stability summary sheets of batch # (b) (4) does not have the confirmed OOS result reported for the related substance test and instead has the repeat analysis results (performed as per No. OOS/20/034) for the 18 month interval.

Add Continuation Page

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parkland Drive, Room 2093 Rockville, MD 20857 Industry Information: www.fda.gov/oc/industry	09 June 2022 to 20 June 2022* FEI NUMBER 3014210753

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Viral Shah, Managing Director

FIRM NAME	STREET ADDRESS
Immacule Lifesciences Private Ltd. India	Village Thanthewal, Ropar Road
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Nalagarh, District Solan, Himachal Pradesh 174 101	Manufacturer

ii. The results were reported prior to completion of the OOS investigation.

iii. The 24-month stability report failed to indicate that the 18 month result was OOS for related substance.

iv. The stability summary sheet for the (b) (4) samples of (b) (4) inaccurately concluded, "The results show that there are no significant physical, chemical and microbial changes when the product is kept at a temperature of 5°C + 3°C for 24 months". The Stability Summary Report for the (b) (4) samples concluded, "The results show that there are significant physical changes when the product is kept at a temperature of 5°C + 3°C for 24 months"

b) The sterility test reports for (b) (4) njection (b) (4) ng batch # (b) (4) and (b) (4) (b) (4) njection (b) nL batch # (b) (4) has "complies documented to the statement of, (b) (4) layer after sterility". On 16 June 2022, samples were seen without a (b) (4) ayer. The missing layer was mentioned in the presence of the Head of QC, but the test results were approved without any further action taken.

2022 CA 28 JUNE 2022

c) CCIT testing on (b) (4) njection (b) (4) ng/ (b) (4) nL ((b) (4) ng/mL) on 10 June 2021 had two failed results documented which required retesting (b) (4) imes of each failing vials. In-Process Quality Assurance (IPQA) approved testing with signature for failing test result for one of the two times vials failed CCIT testing.

d) You have not established acceptance criteria for identifying critical defects during manual optical inspection (visual inspection) qualification for employees. Your Optical Inspection Validation Protocols for both (b) (4) drug product vials and (b) (4) drug product vials, numbers EMVP/GS/22/141 and EMVP/GS/22/139 respectively, state the acceptance criteria for employees to be qualified is for them to detect more than (b) (4) % of all defects and to have no more than a (b) (4) % false rejection rate.

For example, aseptic operator (b) (6) was qualified for optical inspection in May 2021, but he failed to detect glass particles in five (5) (b) (4) filled (b) (4) ml vials out of (b) (4) total vials for this kit type, glass particles in three (3) (b) (4) filled (b) (4) ml vials out of (b) (4) total vials for this kit type, and glass particles in one (1) (b) (4) filled (b) (4) ml vial out of (b) (4) total vials for this kit type. Your firm has identified glass particles as a critical

Add Continuation Page

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Cynthia Jun	Cynthia Jun, CSO Wayne D. McGrath, CSO	06/20/2022

critical defect. The qualification report makes no mention of the missed critical defects, but only states total detection rate and false rejection rate. As of June 17, 2021, aseptic operator (b) (6) has not been requalified for optical inspection.

OBSERVATION # 4

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not followed.

Specifically,

a) Observation of aseptic filling operations on the Vial Filling Line in the (b) (4) restricted access barrier system (b) (4) on 09 June 2022 revealed the following,

i. The transfer of sterilized components into the vial filling (b) (4) unit, including product filling (b) (4) with attached (b) (4) tubes, manifold with (b) (4) tubes for filling (b) (4) with attached (b) (4) tubes and manifold, (b) (4) for (b) (4) and (b) (4) with attached tubes and manifold was observed on 09 June 2022. The sterile components were placed into (b) (4) through open (b) (4) one at a time, with (b) (4) closure after (b) (4) entry. Each sterile component was set up using (b) (4) gloves.

ii. After each sterile component placement, sterile components and (b) (4) gloves were exposed to the (b) (4) RAB (b) (4) and operator intervention without sanitization of the (b) (4) gloves.

iii. The connection of (b) (4) filling (b) (4) with (b) (4) tubing to the valve pumps and the product manifolds requires handling of the sterilized tubing to make (b) (4) connections with (b) (4) gloves.

iv. The sterilized tubing connection from (b) (4) tank to the filling pumps were performed with (b) (4) gloved hands without sanitization of gloves from previous open (b) (4) intervention.

b) SOP/PR/050, Operation & Cleaning of Online Non-Viable Particles, requires that if nonviable particles alarms exceed (b) (4) vials (b) (4) the nonviable particle probe are removed. There is no scientific

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parkland Drive, Room 2093 Rockville, MD 20857 Industry Information: www.fda.gov/oc/industry	09 June 2022 to 20 June 2022* FEI NUMBER 3014210753

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Viral Shah, Managing Director

FIRM NAME	STREET ADDRESS
Immacule Lifesciences Private Ltd. India	Village Thanthewal, Ropar Road
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Nalagarh, District Solan, Himachal Pradesh 174 101	Manufacturer

rationale for the rejection of (b) (4) vials regardless of vial size (diameters ranging from (b) (4) mm to (b) (4) mm) and regardless of the number of unstoppered vials at (b) (4) used for (b) (4) product filling, and (b) (4) (b) (4)

OBSERVATION # 5

Your examination and testing of samples did not assure that the drug product and in-process material conformed to specifications.

Specifically,

a) Sterility testing is not performed in a manner that ensures the growth of anaerobic organisms if present in the sample. SOP/QC/186 Sterility Testing, requires, "During the incubation period and at its conclusion, examine the media for evidence of microbial growth/turbidity on (b) (4) basis". On 16 June 2022, we observed the final reads for a negative control and three product samples for (b) (4) Injection (b) (4) mg batch # (b) (4) and (b) (4) njection (b) (4) mL batch # (b) (4) We observed that the negative control had a clear (b) (4) layer in the upper one-fourth (1/4) of the (b) (4) canister; one product sample in (b) (4) canister had pink color in the upper three-fourths of the canister; and 2 product samples in (b) (4) canisters had pink color throughout the canister indicating presence of (b) (4) hroughout the canister. The sterility test records for the three samples documented presence of (b) (4) layer after sterility" approved by Head of QC on 17 June 2022.

b) Leak testing / container closure integrity testing of filled and sealed vials were not performed according to procedures, SOP/PR/093, "Operation and Cleaning of Leak Testing Machine (b) (4)

i. Not all vials that exceed the specification for leak testing are retested. In-process leak testing is required for (b) (4) vials (b) (4) during filling operations. Vials that exceed the limit for leak testing requires (b) (4) imes retest.

ii. Leak testing of (b) (4) njection (b) (4) ng (b) (4) mL (b) (4) ng/mL), Batch # (b) (4) on 10 June 2021, was not performed according to procedures. Personnel failed to perform retesting of vials that failed leak testing acceptance criteria on (b) (4) separate occasions. At (b) (4) one of (b) (4) vials failed leak testing, but was

one of

Add Continuation Page

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Cynthia Jim	Cynthia Jim, CSO Wayne D. McGrath, CSO	06/20/2022

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parkland Drive, Room 2093 Rockville, MD 20857 Industry Information: www.fda.gov/oc/industry	09 June 2022 to 20 June 2022* FEI NUMBER 3014210753

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Viral Shah, Managing Director

FIRM NAME	STREET ADDRESS
Immacule Lifesciences Private Ltd. India	Village Thanthewal, Ropar Road
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Nalagarh, District Solan, Himachal Pradesh 174 101	Manufacturer

CJ 20 June 2022

retested ~~only~~ once. At (b) (4) one of (b) (4) vials failed leak testing and was not retested. At (b) (4), one of (b) (4) vials failed leak testing and also failed (b) (4) times retest.

c) Procedures to perform leak testing according to SOP-PR-062, Leak Testing Machine, is incomplete. The (b) (4) Leak Testing machine was placed out of service on 30 May 2022, due to "UPS Alarm", and as of 17 June 2022, the unit was still out of service requiring use of the (b) (4) Leak Test Apparatus.

i. SOP-PR-062 does not include the requirement to document the test results for each of the (b) (4) vials. On 17 June 2022, testing of (b) (4) vials was documented as "Accept", but results for each unit tested was not documented.

ii. SOP-PR-062 does not provide instruction on what to do if any vial shows a leak has occurred. There are no instructions for retesting or the necessity to perform leak testing on units between the last passing in-process to current failing in-process check.

OBSERVATION # 6

Verification of the suitability of the testing methods is deficient in that they are not performed under actual conditions of use.

Specifically,

a) Vials that fail that Container Closure Integrity Test are tested for sterility by (b) (4) The sterility test by (b) (4) has not been qualified to capture contamination from one vial or sample size of (b) (4) nL.

b) You have not fully qualified your environmental monitoring using swabs by performing a swab recovery study on all materials being swabbed. According to your procedure, number SOP/QC/025, Viable and Non-Viable Particle Monitoring of Production Formulation Facility, you use swabs to perform environmental monitoring in Grade A and Grade B areas on a variety of surfaces, including, but not limited to, (b) (4) and (b) (4) According to your swab recovery study performed in 2017, you only tested the swabs on

Add Continuation Page

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Cynthia Jim	Cynthia Jim, CSO Wayne D. McGrath, CSO	06/20/2022

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parkland Drive, Room 2093 Rockville, MD 20857 Industry Information: www.fda.gov/oc/industry	09 June 2022 to 20 June 2022* FEI NUMBER 3014210753

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Viral Shah, Managing Director

FIRM NAME	STREET ADDRESS
Immacule Lifesciences Private Ltd. India	Village Thanthewal, Ropar Road
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Nalagarh, District Solan, Himachal Pradesh 174 101	Manufacturer

(b) (4) and (b) (4) Your firm uses (b) (4) tubes in the Grade A area for the aseptic filling of drug products including, but not limited to, (b) (4) Injection USP (b) (4) mg/mL and (b) (4) injectable emulsion USP (b) (4) mg (b) (4) mL. Your firm uses swabs to monitor these (b) (4) tubes for microbial contamination.

OBSERVATION # 7

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

Specifically,

a) Your firm does not perform continuous non-viable particle (NVP) monitoring in each of the Grade A areas during aseptic vial filling operations. Your SOP, number SOP/QC/025, Viable and Non-Viable Particle Monitoring of Production Formulation Facility, only requires (b) (4) monitoring of Grade A areas lacking an online NVP counter. You stated a portable, offline NVP counter is used for these (b) (4) monitoring activities. These areas include the Grade A extended laminar airflow (LAF) area where the (b) (4) tank is stored and the (b) (4) gloves are exposed during set up and the Grade A conveyors in the (b) (4) leading to the (b) (4) and the sealing area. In addition, your SOP states "The non-viable particle monitoring (offline monitoring) of Grade A shall be done when no filling activity is being done." You stated all of the sterile drug products your firm exports to the US are made on the aseptic vial filling line, including, but not limited to, (b) (4) Injection USP (b) (4) mg/mL and (b) (4) USP (b) (4) mg (b) (4) mL.

b) Environmental monitoring of the Grade B production area, surrounding the (b) (4) RABS unit where manufacturing personnel stand or move throughout filling operations, are only monitored at the (b) (4) of filling line set up but not any other time during filling operations.

OBSERVATION # 8

Drug products are not stored under appropriate conditions of temperature so that their identity, strength, quality, and purity are not affected.

Specifically,

Your firm does not continuously monitor the temperatures of the freezers used to store active pharmaceutical

Add Continuation Page

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Cynthia Jim	Cynthia Jim, CSO Wayne D. McGrath, CSO	06/20/2022

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parkland Drive, Room 2093 Rockville, MD 20857 Industry Information: www.fda.gov/oc/industry	09 June 2022 to 20 June 2022* FEI NUMBER 3014210753

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Viral Shah, Managing Director

FIRM NAME	STREET ADDRESS
Immacule Lifesciences Private Ltd. India	Village Thanthewal, Ropar Road
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Nalagarh, District Solan, Himachal Pradesh 174 101	Manufacturer

ingredients (APIs), including, but not limited to, (b) (4) and (b) (4) Your SOP, number SOP/WH/043, Operation and Cleaning of Deep Freezer, states "Temperature recording shall be done (b) (4) " You stated the raw material freezers, equipment numbers WH/FRZ-01 and WH/FRZ-05, are equipped only with audible alarms in the event their temperature exceeds specification, but employees are not always in the area where the freezers are located. The alarms do not electronically notify responsible individuals in the event of a temperature excursion. The temperature set point for Freezer number WH/FRZ-05 is -12 degrees Celsius to -22 degrees Celsius, which is outside the required storage temperature of -15 degrees Celsius to -25 degrees Celsius for API (b) (4)

*DATES OF INSPECTION
06/09/2020(Thu), 06/10/2022(Fri), 06/13/2022(Mon), 06/14/2022(Tue), 06/15/2022(Wed), 06/16/2022(Thu), 06/17/2022(Fri), 06/20/2022(Mon)

20 June 2022

Add Continuation Page

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Cynthia Jim, CSO Wayne D. McGrath, CSO	06/20/2022

20 June 2022