**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 | 09/08/2025-09/18/2025 |
| | FEI NUMBER: 3014210753 |

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Viral Shah, Managing Director

| FIRM NAME | STREET ADDRESS |
|---|---|
| Immacule Lifesciences Private Limited | Village Thanthewal, Ropar, Road, Nalagarh |
| CITY, STATE, ZIP CODE, COUNTRY: Solan, Himachal Pradesh, 174101, India | TYPE ESTABLISHMENT INSPECTED: Sterile Drug Product Contract 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**

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

A. Your Quality Unit failed to ensure that all production and laboratory control operations follow cGMP requirements. Your Quality Unit has not performed the necessary assessments/reviews to ensure that the objectionable practices observed do not negatively affect the quality attributes of your sterile drug products. Moreover, many of the objectionable conditions noted throughout the inspection suggest that personnel may not have the necessary understanding about the importance of ensuring the integrity of the cGMP data and the scientific knowledge with respect to sterile manufacturing processes and related systems to adequately assess the CGMPs.

B. Your Quality Unit does not produce comprehensive environmental trend reports of the controlled areas, including the critical utilities.

Specifically, your environmental trend assessment report, Document No. MVP/GS/25/269/R01 titled "Report for Assessment of Microbial Recoveries in Environmental & Critical Utilities Monitoring and Microbiological Testing (b) (4) "; approved on 05/15/2025 is inadequate. The objective of this assessment is to evaluate the potential hazards associated with microorganisms identified during routine sampling analyses. According to the trend assessment report (document No. MVP/GS/25/269/R01), a total of (b) (4) recoveries (i.e., EM (b) (4) analyses, respectively)

| SEE REVERSE OF THIS PAGE | EMPLOYEE(S) SIGNATURE | EMPLOYEE(S) NAME AND TITLE (Print or Type) | DATE ISSUED |
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| | | Jose E Melendez, Investigator<br>Damaris Y. Hernandez, Investigator<br>Angelica M. Hernandez, Investigator | September 18, 2025 |

were observed (b) (4) However, the trend report does not provide a comprehensive assessment of the sampling locations where recoveries are observed, or the actions taken to reduce the number of events.

**OBSERVATION 2**

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

A. On September 10, 2025, we observed when the manufacturing operator transferred the (b) (4) LAF #31from the sterile room (b) (4) into the vial filling room (b) (4) the operator sanitized the top and upper sides of the (b) (4) LAF with (b) (4) When wiping with the sanitizing agent, we observed the blue marker ink smear from the label located in the top front right side of the (b) (4) LAF onto the (b) (4) surface. Subsequently, blue ink residue was being transferred via the contaminated wipe to other sections of the (b) (4) LAFs front surface as the operator continued sanitizing.

Additionally, on September 15, 2025, we were able to confirm the blue marker used is removable with the same (b) (4) that is used in the filling room. This same marker is used for documenting the sampling locations on the respective environmental monitoring settle plates, active air plates, contact plates, and personnel monitoring plates.

B. During the pre-environmental monitoring performed in the vial filling line, operators did not adequately sanitize the (b) RABs (b) (4) Specifically, on September 10, 2025, after the operator placed the settle plate in the (b) (4) stopper zone, (b) (4) was (b) (4) and was not sanitize. We observed the operator sanitizing the (b) (4) (excluding the (b) (4) Furthermore, the operator did not sanitize (b) (4) which (b) (4) is facing the (b) (4) LAF (PR/LAF-09 (b) (4) Grade B area.

C. There is no comprehensive assessment demonstrating how the airflow pattern in the filling Room (b) (4) (b) (4) Grade B area is affected by personnel present (b) (4) during assembly and filling operations, including manufacturing operators/microbiologists who transfer parts (b) (4) stoppers/intermediate storage/EM plates using the (b) (4) LAF unit (b) (4) respectively.

D. The air flow pattern study [a.k.a. smoke studies] recorded from 2023 to 2025 do not accurately reflect the aseptic conditions that would be expected during the actual commercial manufacturing process. The dates mentioned in the videos are in the D/M/Y format.

a. During the smoke studies video Intervention #(b)(4) associated to Adjustment and Setting of (b)(4) (b)(4) Loader and Unloading (04/04/2025), we observed when (b)(4) in front of the loader (b)(4) exposed to Grade B area were not sanitized adequately prior to (b)(4)

b. Intervention #(b)(4) Transfer of (b)(4) (04-05/12/2023): during the (b)(4) intervention for assembly of the (b)(4) the operator's right arm from wrist to elbow ingresses into the aseptic core of the filling line. Operator is cutting the steril(b)(4) bag reaching near the end of the (b)(4) (b)(4) the operator's outer wrist to their elbow is in contact with the steril(b)(4) bag these areas of the operator are not included in personnel monitoring.

c. Intervention #(b)(4) Transfer of (b)(4) (05/12/2023): we observed operators passing sterile (b)(4) bags containing (b)(4) through the (b)(4) towards the rear of the aseptic core (b)(4) on the rear side.

d. Intervention #(b)(4) Assembly of (b)(4) and forceps stand in front of (b)(4) (24/03/2024): Operator using both hands to enter the (b)(4) with outer garment coming into contact with the (b)(4) that is not sanitized prior to installing the sterilized (b)(4)

e. Intervention #(b)(4) Transfer of (b)(4) LAF PR-LAF-31 from unloading area to filling room (04/12/2023): there is turbulence within the Grade B filling room. In addition, the video is not representative of the commercial activities where the operators are transporting (b)(4) LAF PR-LAF-31 from the unloading area through the filling room towards the filling line. On September 10, 2025, we observed (b)(4) operators having difficulties moving the (b)(4) LAF past (b)(4) towards the filling line for unloading of (b)(4)

f. Intervention #(b)(4) Assembling of (b)(4) connected with (b)(4) tubes (05/12/2023): apparent contact of the (b)(4) with the opening of the (b)(4) tubing during the assembly connection of

the tubing to the (b) (4) In general, the view is obscured when the operator is making the connection of the (b) (4) tubing to the (b) (4) with the (b) (4)

g. Intervention # (b) (4) Assembling of (b) (4) Vessel (12/12/2023): air velocity appears to be too high compared to the other videos observed. No air velocity for this intervention was provided.

h. Interventions # (b) (4) Assembling of (b) (4) vessel and (b) (4) Vessel (12/12/2023): air velocity appears to be too high compared to the other videos observed. No air velocity for this intervention was provided. In addition, at the (b) (4) mark, there is a cut in the video where the operators hand position immediately changed and the time stamp in the video does not reflect the change in video.

i. Intervention # (b) (4) Transfer of stoppers to (b) (4) (12/12/2023): Unable to observe how stoppers were introduced, and it does not demonstrate the flow of the air to the passive air settle plate, additionally, is not a representative of the actual commercial conditions.

j. Intervention # (b) (4) replacement (12/12/2023): Operator enters both arms through the (b) (4) with their outer forearm and gowning coming in contact with the (b) (4) (b) (4) that is not sanitized prior to replacing the (b) (4)

k. Intervention # (b) (4) Adjustment & Setting of (b) (4) loader for loading & unloading (04/04/2025): during the intervention the (b) (4) is within the Grade B area and is not adequately sanitized prior to being re-introduced to the Grade A area.

l. There is no airflow pattern assessment for the following corrective (b) (4) interventions (i.e., sensor malfunction, (b) (4) loader adjustment and configuration, (b) (4) stuck in the (b) (4) (b) (4) malfunction) that can be performed on the vial filling line. According to the Site Quality Head, these corrective (b) (4) interventions were validated in the following aseptic process simulations (b) (4) respectively; therefore, if required during commercial filling, manufacturing operators may perform them.

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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.**

Aseptic processing operations conducted in filling Room (b) (4) are deficient in design and controls to prevent microbiological contamination of sterile drug products.

For example, on September 8, 10, and 11, 2025, we evaluated the (b) (4) vial filling line (Equipment ID (b) (4) used to manufacture (b) (4) aseptic fill, and terminally sterilized drug products that are manufactured for the USA Market. The following examples of poor filling room design, operators' aseptic behavior, filling line assembly and smoke studies are not an exhaustive listing of what was observed:

A. Your firm's aseptic vial filling line was observed to experience frequent (b) (4) interventions in the ISO 5 (Grade A) filling line area causing multiple line stoppages.

1. (b) (4) Injection (TS), Batch (b) (4) During the filling of this batch, we observed the inherent interventions (Intervention # (b) (4) "handling of rejection of un-stoppered vials/fallen filled vials" (b) (4) times) and (Intervention # (b) (4) "picking up of fallen vials from the (b) (4) conveyor" (b) (4) times), respectively.

2. (b) (4) Injection (TS), Batch (b) (4) During the filling of this batch, we observed the inherent intervention (Intervention # (b) (4) "picking up of fallen vials from the (b) (4) conveyor" (b) (4) times).

The current validated frequency of the referenced inherent interventions for aseptic filling is:

- Intervention # (b) (4) "handling of rejection of un-stoppered vials/fallen filled vials"; (b) (4) times.
- Intervention # (b) (4) "picking up of fallen vials from the (b) (4) conveyor"; (b) (4) times.

The referenced validated frequency suggest that the operators repeatedly must reach into the ISO 5 (Grade A) filling line area to clear fallen or stuck vials, indicating the filling process relies on excessive operators' interventions inside the aseptic zone.

B. There is no assurance that the current flow of personnel within the vial filling Room (b) (4) is designed to prevent microbial contamination.

1. Your current operations and layout of the filling line does not provide adequate separation as seen when personnel transfer the sterilized machine parts and equipment in the (b) (4) laminar airflow (LAF) (b) (4) LAF #19 and (b) (4) LAF #31). Personnel are required to maneuver the (b) (4) LAFs through constricted spaces that compromise the aseptic conditions. This was seen when transporting the (b) (4) LAF #19 from the rear side of the filling line through the (b) (4) conveyor (b) (4) The conveyor connects the stoppering zone with the (b) (4) capping/sealing zones. The manufacturing operators and microbiologist must cross the conveyor with the (b) (4) LAF unit (b) (4) respectively, multiple times to transfer parts (b) (4) stoppers (b) (4) tank/environmental monitoring (EM) plates. Moreover, there is no monitoring of non-viable particles (NVP) during conveyor crossing, even though manufacturing operators constantly enter and exit the (b) (4) LAFs located along the filling line. In addition, excessive physical manipulation of the (b) (4) LAF #31 was seen when operators pushed and pulled the (b) (4) LAF (b) (4) that was being introduced into the vial filling room. The manufacturing operators' movements in the critical areas were not always slow and deliberate.

2. We also observed the (b) (4) LAF #31 originating from Grade B area making physical contact (the top part of the (b) (4) LAF) with the (b) (4) LAF (PR/LAF-21 (b) (4) LAF) from Grade A area. Furthermore, visible damage including dents and scratches on the outer surface of the (b) (4) LAF #19 was observed.

3. On September 11, 2025, during the filling and during the line clearance of (b) (4) Injection Batch # (b) (4) we observed a (b) (4) residue along the tops of the (b) (4) Your Managing Director stated it is a normal occurrence for the active ingredient to (b) (4) He also added that

there is no intervention for wiping the (b) (4) during manufacturing.

4. Procedure SOP-PR-104 titled "Transfer and assembly of Vial filling and Cap sealing machine (b) (4) " version E7, was not followed as Step (b) (4) specifically requires passing the sterile (b) (4) through their respective designated (b) (4) Nonetheless, on September 10, 2025, during the assembling process of vial line, we observed your operators passing the sterile (b) (4) and machine equipment parts through the (b) (4) that were not designated. The sterile (b) (4) and machine equipment parts were transferred from the front side of the filling vial line towards the rear side of the line. The sterile (b) (4) and machine equipment parts were subsequently placed in the (b) (4) and in the (b) (4) within the ISO 5 environment. We also observed your operator forcibly pulling out the sterile (b) (4) from the (b) (4) bag during the installation of (b) (4) on (b) (4) using (b) (4) (b) (4) The sterile (b) (4) bags used to transport machine parts and sterile (b) (4) were removed from the filling line through (b) (4) that had not been sanitized.

**OBSERVATION 4**

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

A. Your firm failed to conduct a scientific rationale for the (b) (4) non-viable particle counter (NVPC) locations (b) (4) within the aseptic core and along the vial conveyor of your (b) (4) vial filling Line (Equipment ID (b) (4) used to manufacture (b) (4) aseptic fill, and terminally sterilized drug products that are manufactured for the USA market. Your Site Quality Head confirmed that your firm has not conducted a risk analysis to determine whether the current locations of the isokinetic probes are meaningful.

Additionally, your "General Validation Report of Worst Case study for Non-Viable Particle Counter Location" Document# MVP/GS/22/236/R01, approved on July 08, 2022, is inadequate as it failed to include and evaluate up to (b) (4) of track of the filling line where (b) (4) product is (b) (4) (b) (4) (b) (4) in-transit to the (b) (4) This protocol does not define how the transport of the (b) (4) (b) (4) vials and any possible operator interventions including the frequency, duration, and flow of (b) (4) vials were evaluated to determine the lack of monitoring.

B. Your firm failed to provide a scientific rationale for the locations selected for settle plates used for passive air monitoring during your assembling activities, commercial filling, and post filling monitoring. We observed a

settle plate under the (b) (4) which, during commercial operations, is completely covered by the sterilized (b) (4) bags filled with stoppers. This set up with the sterilized (b) (4) bags impedes the air from reaching the settle plate during the entirety of your commercial filling activities.

Additionally, a similar deficiency was observed within the (b) (4) LAF #31 that is used during the transfer of materials during your filling vial line assembling activities. This (b) (4) LAF contains a (b) (4) that is completely lined with materials reaching past the halfway portion of the interior height of the (b) (4) Your Deputy General Manager Microbiologist stated, they perform passive air monitoring within the (b) (4) LAF under the (b) (4) and on the (b) (4) before all the materials are transferred from the (b) (4) LAF to the filling line. This practice does not provide any environmental monitoring of your firm's current aseptic practice.

C. Your EM program does not cover all critical surfaces. Specifically, your EM program describes in the control procedure SOP/QC/025 titled "Viable and Non-Viable Particle Monitoring of Production Formulation Facility", Version E15, does not consider the (b) (4) LAF (b) (4) handles as a sampling location. During your commercial filling setup activities, your operators are in continuous contact with their (b) (4) hands on the handles of both (b) (4) LAFs (b) (4) LAF #31 and (b) (4) LAF #19) while removing sterilized items and equipment to be placed into the aseptic core of your filling line while under the (b) (4) LAF.

**OBSERVATION 5**

**Procedures designed to prevent microbiological contamination of drug products purporting to be sterile did not include adequate validation of the aseptic process.**

1. Your aseptic process simulation is not representative of commercial batches release for the USA market.

   For example, your firm uses multiple vial sizes (e.g., (b) (4) in its commercial batches. According to your Site Quality Head, your firm follows the "bracketing" approach to perform the (b) (4) simulations of your commercial aseptic process. However, your firm did not provide a formal risk assessment that considers all potential contamination risk factors that could occur on the vial filling line to justify such a "bracketing" approach. Moreover, during the period between January 2023 and June 2025, approximately (b) (4) % of your USA released batches were filled in (b) (4) mL (b) (4) mm vials. The last time this vial size was evaluated during an aseptic

process simulation was on July 02, 2021 (Media Fill Batch Record # (b) (4)

2. Your firm does not perform a trend analysis of the operators' interventions during the filling of terminally sterilized (TS) drug products.

   Your (b) (4) vial filling line (Equipment ID (b) (4) is used to manufacture (b) (4) aseptic fill, and terminally sterilized drug products for the USA Market. Nevertheless, (b) (4) interventions performed during the commercial filling of TS products are not considered for the media fill design of aseptic filling drug of products, even if the filling of TS products occurs on the same filling line, by the same operators, and using the same primary packaging materials. The lack of trending for the (b) (4) interventions in TS products (i.e., inherent and corrective) does not drive corrective and preventive actions to optimize your filling process by reducing the number of (b) (4) interventions. Additionally, it does not ensure that your aseptic process simulations are representative of commercial issues that may also occur during aseptic filling of sterile liquids (b) (4) products.

**OBSERVATION 6**

**Appropriate controls were not exercised over computerized systems to ensure that changes in records are made only by authorized personnel.**

Your Quality Unit failed to establish sufficient controls, which prevents raw data and recipes/machine operational parameters from being manipulated in the LIMS, and SCADA systems, respectively.

Specifically, we found that your SCADA system had user accounts with extensive administrative privileges, including the ability to modify/edit critical process parameters and recipes without adequate oversight. Additionally, a similar deficiency was observed in LIMS, in which we found that certain users have the privilege and roles to editing or removing data and system parameters that do not pertain to the scope of their responsibilities.

The systems mentioned below are not an exhaustive listing of the systems we observed within your facility, we observed the following deficiencies:

A. The LIMS system is utilized by your Quality Control Lab to input data and at times record raw data that are used to determine the final disposition of a batch of sterile finished product and to transcribe that same data onto a certificate of analysis. Currently, your firm has four (4) levels of access (1 Analyst, 2 Supervisor, 3 Manager, 4 QA) with increasing permissions according to the respective roles. On September 8, 2025, we confirmed that your LIMS Document Manager/Executive with Level 1 Analyst access was able to make changes to the pH result for a drug product that was currently (b) (4) (b) (4) Your Associate Vice President confirmed the LIMS Document Manager/Executive and one other person with this access are not reviewers or analysts. Your Associate Vice President stated the system only has four (4) levels of access and they deemed the first level (analyst) to be appropriate as a "general access" role.

B. The SCADA system is utilized by your production personnel and Quality Assurance to communicate with the equipment in the filling suite to input parameters, execute recipes, and monitor equipment usage. We confirmed that those with administrative access (including you IT and engineer personnel) to the system can make changes to existing recipes by changing equipment parameters.

C. The LabSolutions system in your Quality Control Lab is utilized for documenting in-process, finished product testing, and method validation/transfer. This system is used for the following equipment: HPLC, analytical balances, GC, and TOC. When reviewing the audit trail we observed a "Guest" role that was confirmed to be recently added to identify customers and service providers that have had access to the system for, as your management has stated, method transfer purposes and equipment maintenance/calibrations. Your Associate Vice President stated the "guest" role was added recently to identify these users as stated in your procedure SOP-QC-182 titled "User Privileges and Review of Audit Trail for Critical Instrument", version E20. Prior to the addition of the "guest" role, the customers and service employees, were provided with the role of "Analyst." Within your audit trail, your Associate Vice President separated (b) (4) users, (b) (4) were identified as customers for method transfer and (b) (4) (b) (4) was a service provider who had the role of "Analyst" assigned to them as they were working within your QC lab for an unspecified amount of time. Within this role, these users had the permissions to modify sequence from finish product, in-process, stability, and raw material testing results compromising the integrity and traceability of the data being recorded.

Your firm's Quality Unit failed to review audit trails associated with (b) (4) integrity testing as part of the approval process. Specifically, your Quality Assurance personnel have access and privileges to view audit trails generated

in (b) (4) software for PR(b) (4)-03, however, for PR(b) (4)-02, your QA personnel don't have access and privileges to view the audit trail. Moreover, your procedure SOP-QA-092, "Operation and Cleaning of (b) (4) Integrity Tester (b) (4)", Version E4, does not require QA to review the electronic audit trail when approving the results of the (b) (4) integrity testing. As per your Quality Assurance personnel and procedure mentioned previously, QA approvals are based solely on the result reports without ensuring changes, failed tests and/or repeated runs are evaluated prior to and/or post to using the (b) (4) in the manufacturing of your drug product. Furthermore, your Quality Assurance management/personnel stated your IT personnel who has administrative rights in (b) (4) software prints the audit trail (b) (4) and provides it to QA for their approval.

**OBSERVATION 7**

**There is a failure to thoroughly review any unexplained discrepancy or the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.**

You failed to consistently conduct adequate laboratory investigations. Specifically, your investigations lack data supporting the assigned root cause(s).

A. Investigation OOS/24/001 was initiated on April 11, 2024, due to an action-level result of (b) (4) CFU in volumetric air sampling during routine pre-environmental monitoring (EM) of the vial line (Equipment ID (b) (4) in preparation for line setup for (b) (4) injection USP (b) (4) mg, Batch (b) (4) (No USA distributed drug products). The recovery was observed at the ISO-5 sampling location (b) (4) identified as (b) (4) (b) (4) The observed recovery was identified as *Kocuria rosea*, which is common human skin microflora.

Additionally, recoveries were observed in the Grade B and Grade C areas for settle plate exposure, volumetric air sampling, surface monitoring, and personnel monitoring during commercial aseptic filling activities for Batch (b) (4) please see the table below for reference:

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| Location ID (Grade) | Total No. of Colonies | Identification Result |
|---|---|---|
| **Settle Plate Exposure** (b) (4) | | |
| [redacted] | | |
| **Volumetric Air Sampling** (b) (4) | | |
| [redacted] | | |
| **Surface monitoring** (b) (4) | | |
| [redacted] | | |
| **Personnel monitoring** (b) (4) | | |
| [redacted] | | |

| | EMPLOYEE(S) SIGNATURE | EMPLOYEE(S) NAME AND TITLE (Print or Type) | DATE ISSUED |
|---|---|---|---|
| SEE REVERSE OF THIS PAGE | AMH | Jose E Melendez, Investigator<br>Damaris Y. Hernandez, Investigator<br>Angelica M. Hernandez, Investigator | September 18, 2025 |

Investigation OOS/24/001 concluded that, during handling of the air sampler, the operator's garments contacted the filling laminar airflow (LAF), which can cause particle shedding or contamination. However, none of the samples collected from the operators' garments showed any recovery, except for the booties. Based on this preconceived root cause, your firm eliminated the active air sampling before clearing the line for the assembly of machine parts from the routine EM. With this action, your firm is not taking active air sampling during the pre-assembly activities of the filling vial line (b) (4) interventions). This (b) (4) intervention lasts between (b) (4) and (b) (4) according to aseptic process simulations. Currently, this monitoring is performed after the installation of the (b) (4) in the (b) (4) interventions). Your Quality Unit released (b) (4) Injection USP (b) (4) mg, Batch (b) (4) and did not include it on the stability program.

B. Laboratory Investigation INV/OOS/25/028, dated July 28, 2025, for (b) (4) Injection USP (b) (4) mg/mL, Batch (b) (4) was initiated when the assay (by HPLC) result was found Out-of-Specification (OOS) (b) (4) % and (b) (4) %; Mean (b) (4) %) against the specification range of (b) (4) % to (b) (4) %) at in-process stage (b) (4) bulk sample). Your investigation inferred that the most probable cause is dilution error during sample preparation, as reinjection of the original vial and injection of a new vial with the same sample solution confirmed the initial OOS result. Your Quality Control (QC) laboratory invalidated the original assay OOS result, performed a reanalysis in triplicates of Batch (b) (4) and then reported the results of the repeat analysis. Your investigation is inadequate in that the most likely cause identified was not simulated as part of your laboratory investigation process. Furthermore, only the sample that showed an OOS result was reanalyzed. The other samples analyzed by the same analyst with the same HPLC sequence was not considered for reanalysis.

C. Laboratory Investigation INV/OOS/25/005, dated February 27, 2025, for (b) (4) (b) (4) Injection, Batch (b) (4) was initiated when the assay (by HPLC) result was found OOS (b) (4) %) against the specification range of (b) (4) % to (b) (4) %) at finished product stage (after sealing and visual inspection (b) (4) Your investigation inferred that the most probable cause is pipetting error during the sample stock preparation. A hypothesis study plan was conducted to confirm the identified root cause. Two (2) samples of Batch (b) (4) were prepared with Sample 1 as "correct pipetting" and Sample 2 as "suspected pipetting error". Your Quality Control (QC) laboratory invalidated the original assay OOS result, based on the OOS result obtained (b) (4) %) from Sample 2 of the hypothesis study. However, your INV/OOS/25/005 is inadequate because it does not include an accurate

simulation of the pipetting error, as no description of the sample preparation is included.

D. Laboratory Investigation INV/OOS/23/037, dated November 21, 2023, was initiated for (b) (4) (b) (4) Emulsion, USP (b) (4) mg/mL (Batch (b) (4) due to an out-of-specification (OOS) result obtained during the 18-month-long-term stability conditions (25°C/60% RH), for (b) (4) (b) (4) testing (b) (4) against the specification of not more than (NMT) (b) (4) The sample was tested at an external contract laboratory that initiated the investigation and conducted three experiments. Two experiments yielded inconclusive results because they demonstrated passing outcomes, preventing the external contract laboratory from confirming the OOS result. The third experiment was conducted under controlled temperature conditions and yielded passing results, leading the external contract laboratory to conclude that the OOS was associated with transportation conditions. However, the firm had previously released (b) (4) batches without temperature monitoring during transportation, and no OOS results were obtained for those batches.

**OBSERVATION: 8**

**Employees engaged in the manufacture, processing, packing and holding of a drug product lack the education, training and experience required to perform their assigned functions.**

Your firm utilizes visual inspection kits (b) (4) Kits) for some configurations of select drug products including vials destined for the U.S market consisting of the same configuration: (b) (4) vials with (b) (4) rejects with the following reject groups of (b) (4) major, (b) (4) minor, and (b) (4) critical. This set up configuration of your test kits has not undergone any change within, at least, the past seven (7) years. When your operators complete their training/qualification/re-qualification, they receive a Certificate for Optical Inspector Qualification (SOP/QA/103-F06) in which a percentage of the acceptance criteria is documented, signifying if the operator is qualified or not. We reviewed qualification certificates for (b) (4) operator from (b) (4) operators from (b) (4) and (b) (4) operators from (b) (4) all the results for each of these operators were the following: 100% for critical rejection, 100% for major rejection, and 100% for minor rejection. These operators are considered qualified to perform the 100% (b) (4) visual inspection on all products manufactured, including US product, at your facility.

**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 | 09/08/2025-09/18/2025 |
| | FEI NUMBER: 3014210753 |

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Viral Shah, Managing Director

| FIRM NAME | STREET ADDRESS |
|---|---|
| Immacule Lifesciences Private Limited | Village Thanthewal, Ropar, Road, Nalagarh |
| CITY, STATE, ZIP CODE, COUNTRY: Solan, Himachal Pradesh, 174101, India | TYPE ESTABLISHMENT INSPECTED: Sterile Drug Product Contract Manufacturer |

Additionally, you do not have any scientific rationale to support the qualification of your operators with kits that are not a representative of your worst-case products such as the (b) (4) Injection USP which is described as a "(b) (4) solution filled in (b) (4) glass vial" in which (b) (4) is defined by your Managing Director as "(b) (4)" This product is currently within expiry and distributed to the USA Market.

NIA
09/18/25

| | | | |
|---|---|---|---|
| SEE REVERSE OF THIS PAGE | EMPLOYEE(S) SIGNATURE | EMPLOYEE(S) NAME AND TITLE (Print or Type): Jose E Melendez, Investigator; Damaris Y. Hernandez, Investigator; Angelica M. Hernandez, Investigator | DATE ISSUED: September 18, 2025 |

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."