DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
CBER/OCBQ/Division of Manufacturing and Product Quality 10903 New Hampshire Avenue Silver Spring, MD 20993 Lead Inspector: Holly Brevig TEL: 301-796-0742 Industry Information: www.fda.gov/oc/industry	05/26/2025-05/30/2025 FEI NUMBER 3026042970

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED	
Wade Macedone, Chief Executive Officer	
TO: FIRM NAME Andelyn Biosciences, Inc.	STREET ADDRESS 1180 Arthur E. Adams Drive
CITY, STATE, ZIP CODE, COUNTRY Columbus, OH 43221 USA	TYPE ESTABLISHMENT INSPECTED Drug Substance 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

Quality oversight is inadequate to ensure (b)(4) drug substance (DS) has the (b)(4) it purports or is represented to possess. For example,

a. Your quality unit does not review production records adequately to ensure there are no errors that have occurred. Master Batch Records (MBRs) have (b)(4) undergone complete review and sign-off by Quality Assurance followed by re-review after additional issues are identified that require corrections and notations.
b. Lots (b)(4) and (b)(4) have been re-dispositioned three times after the initial batch release due to identification of additional deviations subsequent to batch disposition.
c. Deviation management is inadequate to demonstrate quality oversight of the manufacturing process and does not adequately identify, document, or investigate the impact to (b)(4) DS. For example,
    i. Deviations from written production procedures are not identified as deviations, and procedures governing deviations are not followed. For example,
        1. During performance of MBR (b)(4) for lot (b)(4), it was noted that the (b)(4) did not have the appropriate (b)(4) connector to connect to the (b)(4)

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	Holly N. Brevig -S Digitally signed by Holly N. Brevig -S Date: 2025.06.20 08:27:25 -04'00' SUSAN BUTLER -S Digitally signed by SUSAN BUTLER -S Date: 2025.06.20 12:55:51 -04'00' Jacob L. Bitterman -S Digitally signed by Jacob L. Bitterman -S Date: 2025.06.20 09:41:01 -04'00'	Holly Brevig, CSO, Lead Inspector Susan S. Butler, Staff Fellow Jacob L. Bitterman, Biological Reviewer	05/30/2025

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Additional materials were brought into the manufacturing suite to transfer (b)(4) to another (b)(4) for use during the (b)(4) process. This was documented as a comment on the batch record and brought to the deviation review board. The deviation review board noted that the procedure would need to be modified for all PPQ batches but did not determine that this was a deviation. No investigation, root cause analysis, or corrective and preventive action (CAPA) was performed.

2. During performance of MBR (b)(4) for lot (b)(4), a (b)(4) (b)(4) connection was (b)(4) onto a (b)(4). However, the procedure required a (b)(4) connection, and alternative connections were not described in the procedure. The process proceeded, and the use of the (b)(4) connection was documented as a comment on the batch record and brought to the deviation review board. The deviation review board determined this was not a deviation, despite SOP- (b)(4), Deviation Management, defining a deviation as "any departure from an approved instruction or established standard (e.g., SOP, (b)(4) Master Batch Record, Specification, Analytical Method, or regulatory requirement)." The review board determined that this incident did not indicate a deviation, and there was no investigation, root cause analysis, or proposed CAPA.
3. During performance of MBR (b)(4) for DS (b)(4) lot (b)(4) on (b)(4) /2025, a new (b)(4) (b)(4) Assembly on the (b)(4) (b)(4) was needed due to a failed connection. While this incident was denoted in MBR and initialed by Quality Assurance (QA) on (b)(4) /2025 and conveyed to the deviation review board on time (b)(4) (b)(4), a deviation was not opened by the deviation review board as of (b)(4) /2025, as the board is deciding if this incident is a supplier corrective action request (SCAR) governed by SOP- (b)(4)

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(b)(4) Supplier Management. Neither the Supplier Management SOP nor the Deviation Management SOP (SOP-(b)(4)) contain sufficient detail regarding the pathway to decide if a deviation or SCAR should be opened

4. Deviation investigations are inadequate and effective CAPAs were not implemented to prevent recurrence. For example, DEV-00981 (opened 9/24/2024) was opened per client's request to initiate a trend for deviations attributed to human error (pertinent to the manufacture of (b)(4) DS PPQ 1 and PPQ 2). Although change controls CR-01520 and CR-01672 were opened as a result of this deviation to update batch records, there were no CAPAs initiated and no effectiveness checks occurred. Human error deviations persisted throughout PPQ3 (e.g., DEV-01258, DEV-01242, DEV-01236, DEV-01206, DEV-01148).

d. Unplanned maintenance events are not reviewed by your quality unit, nor are they addressed in a timely manner. For example, Work Order MWO-003630-2024 for remediation of the (b)(4) surface opened on 6/6/2024 has not been closed.

e. Documentation practices are inadequate to ensure (b)(4) drug substance (DS) has (b)(4) it purports. For example,

i. An uncontrolled spreadsheet, described as the "document tracking index" in SOP-(b)(4), Generation and Issuance of Batch Records, is used to document issuance and archival of batch records. Modifications made to this spreadsheet are not attributable to a specific individual.

ii. Controlled documents are not adequately reviewed before they are approved and put into effect. For example:

1. MBR (b)(4) and form SOP-(b)(4) were approved as effective versions with the incorrect version number indicated in the header. Operators manually corrected the version numbers by making notes on the documents. Despite these corrections being required on multiple forms, a deviation was not opened, an investigation was not conducted to identify

potential additional forms with similar errors, and no CAPAs were initiated.

2. MBR-(b)(4) includes a (b)(4) transfer log as Table (b)(4) The table includes item numbers (b)(4) and (b)(4) (b)(4) that are different from the item numbers indicated for the same materials (b)(4) in the bill of materials contained in Section (b)(4) of the batch record. Operators crossed out and corrected the incorrect item numbers with a note on the batch record.
3. Due to incomplete signature dating which included the month and year only, it is not clear whether QA reviewed the validation protocol VP-000350v1 prior to execution.
4. Protocol (b)(4) used for the qualification of (b)(4) (b)(4) incubators was conducted using templates designed for the qualification of freezers.

f. Training is inadequate. SOP-(b)(4), Training of Personnel, does not cover the entire training process. For example, on the job training may encompass only a subset of a given process, as opposed to an entire operation. Therefore, there is not the assurance that personnel are comprehensively trained on a given activity. Additionally, there is not designated qualified trainers to evaluate the on the job training.

OBSERVATION 2

Environmental monitoring program is deficient to ensure environments are classified and controlled to manufacture (b)(4) DS. For example,

a. Validation of the environmental monitoring (EM) sampling for viables has not been conducted. For example, EM samples for viables are transported to an off-site testing facility; however, no studies have been conducted to assess the impact of this process on microbial recovery.
b. There was no non-viable particulate monitoring of the ISO (b)(4) during the manufacturing activities for the processing of (b)(4) DS PPQ lots.

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c. The environmental monitoring program qualification (EMPQ) did not adequately qualify the maximum allowable number of personnel in areas used to manufacture (b)(4) (b)(4) DS. The maximum number of personnel was not challenged for (b)(4) runs.

OBSERVATION 3

Qualification of areas used to manufacture (b)(4) DS is not adequate. Specifically,

a. Cleanroom recovery tests do not support your delay for differential pressure alarms contained in the building management system (BMS) (b)(4). Specifically, you retain a delay setting for differential pressure alarms of (b)(4) despite the cleanroom installation and operational qualification (IOQ) demonstrating a much more rapid room recovery time (e.g., the IOQ for clean room suite (b)(4) recovers in less than or equal to (b)(4)). Thus, the differential pressures failures in areas used to manufacture (b)(4) drug substance are not investigated.
b. The Air Handling Unit (AHU (b)(4) covers the Grade (b)(4) and the Grade (b)(4) (b)(4) However, the qualification failed to evaluate all rooms supplied by AHU (b)(4). For example, Rooms (b)(4) and (b)(4) were not included in the cleanroom qualification. Therefore, there is insufficient data to demonstrate that these rooms are in a state of control.
c. Diagrams supporting airflow into cleanrooms are deficient. For example, document H-01-000-621 in support of airflow of cleanroom suite (b)(4) does not demonstrate a scientifically founded air balance. Thus, the documentation does not support adequate airflow suitable for supporting the respective cleanroom.

OBSERVATION 4

Monitoring of utilities is deficient. For example,

a. Critical product contact (b)(4) used in the manufacture of (b)(4) DS is not adequately qualified or (b)(4) monitored. Specifically, incoming quality control testing is not performed on the (b)(4) received from the vendor, and (b)(4) monitoring program has not

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been established for this utility that is supplied throughout the facility by (b)(4). Furthermore, utilization of (b)(4) has continued in the absence of a complete qualification of the system.

b. (b)(4) water used in (b)(4) incubators, which is changed (b)(4), is not controlled for bioburden. Specifically, incoming (b)(4) water does not have a bioburden specification on the certificate of analysis, and no incoming testing is performed. The incubators are used to support the (b)(4) used in the manufacture of (b)(4) DS.

OBSERVATION 5

Disinfectant efficacy studies are inadequate to mitigate contamination and cross-contamination. For example,

a. The disinfection efficacy study does not demonstrate effectiveness against viral contaminants.
b. The disinfection efficacy study does not demonstrate effectiveness against microbial agents for all representative surfaces in areas used to manufacture (b)(4) DS. For example, the (b)(4) that are used to transport material into and out of cleanrooms and store (b)(4) were excluded from the study.

OBSERVATION 6

Procedures regarding out of specification results described in SOP-(b)(4), Laboratory Investigation Management, are inadequate. The procedures have insufficient detail regarding when expanded investigational activities will be required, how hypothesis testing or retesting investigations will be designed, or how results of the expanded investigational activities will be used to make decisions.

***DATES OF INSPECTION**
05/26/2025 (Mon), 05/27/2025 (Tue), 05/28/2025 (Wed), 05/29/2025 (Thu), 05/30/2025 (Fri)

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

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

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

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