DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
CDER/OPQ/OPMA 10903 New Hampshire Avenue; White Oak Building 51/Room 2269 Silver Spring, MD 20993-0002 E-mail: OPMABLAInspection483Responses@fda.hhs.gov	06/26/2025 -07/04/2025
	FEI NUMBER 3013702557

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Robert Wessman, CEO

FIRM NAME	STREET ADDRESS
Alvotech HF.	Saemundargata 15-19
CITY, STATE, ZIP CODE, COUNTRY Reykjavik, 102, Iceland	TYPE ESTABLISHMENT INSPECTED Drug Substance and 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

Your firm failed to establish written procedures for production and process controls designed to assure that the drug products have the identity, strength, purity, and quality that they are purported or represented to possess.

Specifically,

Per SOP-0832 (b) (4) Application (b) (4) Filling Equipment" (version 5.0, effective 04 Apr 2024), (b) (4) s applied to (b) (4) multiple indirect product-contact stopper delivering and stoppering parts (including (b) (4) used during the filling and stoppering of (b) (4) (b) (4) You have not provided adequate data and scientific justification to demonstrate that this (b) (4) application is consistently controlled and would not adversely impact product quality and stability.

Observation 2

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

Specifically,

A. Since January 2025 you received 159 complaints for (b) (4) associated with (b) (4) You identified an increased trend for (b) (4) product complaints, with similar complaints categorized as (b) (4) (b) (4) (use error)" and (b) (4) and trended separately. You did not provide scientific justification for trending these complaints separately or documentation defining a (b) (4) complaint, (b) (4) complaint or how user error is determined. Although none of these complaint categories reached the upper control limit (UCL) of natural variation when analyzed individually, the UCL was exceeded when the complaints were analyzed together. No evidence was provided that this upward trend was evaluated prior to 23 Jun 2025, no CAPA was raised until 03 Jul 2025, and no supplier investigation has been opened with the (b) (4) supplier or (b) (4) as of the closeout of the inspection on 04 Jul 2025.

B. Not all drug substance (DS) lots are withheld from use until the lots have been fully reviewed and

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SEE REVERSE OF THIS PAGE		Ekaterina Allen, PhD, Pharmaceutical Scientist Leiyun Boone, PhD, Lead Biologist Kathryn King, PhD, Biologist Hyung-yul Lee, Ph.D, Pharmaceutical Scientist Della Shin, PhD, Pharmaceutical Scientist Zhong Li, Ph.D., Senior Regulatory Specialist	July 4, 2025

released by the quality control unit. Per SOP-1680 '(b) (4) Processing of Drug Substance / Drug Product" Ver 10.0 (Effective Date 19 Nov 2024), drug substances can be (b) (4) processed (b) (4) (b) (4) for filling into drug product (DP) lots, without obtaining unprocessed bulk virus testing results and without the completion of all associated document and data reviews by your quality unit.

C. There was a lack of quality oversight for the planning and initiation of an additional (b) (4) PPQ runs as documented in DEV-003670. These runs were planned prior to closure of all deviations associated with the previous failed PPQ batches, and without adequate justification and documentation.

D. A quality agreement between your firm and the applicant of the (b) (4) for (b) (4) DS and DP manufacture was not in place at the start of the inspection. Specifically, the responsibilities of the quality unit of the (b) (4) sponsor for the quality of the (b) (4) are not described in writing.

Observation 3

There is a lack of assurance that your drug substance and drug product manufacturing operations are appropriately designed to ensure the prevention of contamination of equipment or product by environmental and processing conditions that would be expected to have an adverse effect on product quality.

Specifically,

A. The microbial controls of your DS manufacturing process are deficient. For example,

i. You do not have adequate microbial control of your (b) (4) unit operation. Twenty (20) bioburden excursions in (b) (4) intermediates in (b) (4) and (b) (4) viral inactivation unit operations were identified in PPQ and post-PPQ batches. Additionally, nineteen (19) bioburden failures were observed in (b) (4) samples, including (b) (4) after storage, for (b) (4) used in manufacture of (b) (4) products.

ii. You provided evidence of filamentous fungi recovery from the product stream of (b) (4) and (b) (4)

Date	Batch	Sample	Recovery
(b) (4)			

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[redacted]

Additionally, you recovered [redacted] CFU of *Sarocladium kiliense* from [redacted] cleaning sample collected during [redacted] lot manufacture.

iii. [redacted] used for [redacted] of [redacted] are sampled for bioburden out of storage following [redacted] CV of [redacted] There is no assurance that the obtained results are reflective of the bioburden levels of the [redacted]

iv. On 01 July 2025, I (EA) observed collection of bioburden release sample of final formulated bulk of [redacted] batch [redacted] that was performed at the beginning of bulk DS filling operations, [redacted] of the [redacted] The sample is not representative of the microbial levels of the formulated bulk at the end of hold.

v. The established microbial sample hold times for your bioburden and endotoxin samples is NMT [redacted] You calculate sample hold time from the time of sample submission for testing and not from the time of its collection.

B. The environmental control of the classified process areas in your DS and DP manufacturing facilities is deficient. This is evidenced by:

i. Classified areas of your facility exhibit consistently elevated microbial contamination recovery rates (CRR). For example, the following trends were observed in 2024:

a. CRR over [redacted]% were observed for various sample types in Grade B side of entry [redacted] in Feb-Dec 2024 (up to [redacted]%).

b. Grade C areas in [redacted] facility exhibited persistently high contamination recovery rates. For example, Grade C side of the entry [redacted] Change Room exhibited contamination levels of [redacted]% in Feb-Dec 2024.

c. Mold and filamentous fungi were repeatedly detected in classified areas of your facility from January 2023 through December 2024 including recurrent recoveries in room [redacted] (DEV-003110 and DEV-003253) and room [redacted] (DEV-003330 and DEV-004227). A total of 13 associated deviations were opened, of which 11 deviations were deemed isolated events and closed without a CAPA being implemented. You have recently raised 14 CAPAs for contamination control program improvement. At the close out of the inspection on 04 Jul 2025 several CAPAs are pending implementation or are pending an effectiveness check.

ii. Your alarms for differential pressure between areas of different classifications in your sterile

drug product process areas are not appropriately established to ensure that at least (b) (4) Pa positive pressure differential is maintained between adjacent rooms of differing classification (b) (4) Lower limit differential pressure alarms from the (b) (4) Filling room (Grade B) to the (b) (4) (Grade B/C), from the (b) (4) to the (b) (4) (Grade C/D), and from (b) (4) to (b) (4) corridor are set at (b) (4) Pa each. The lower limit differential pressure alarms from the (b) (4) Filling room (Grade B) to the (b) (4) (Grade C/D) is set at (b) (4) Pa.

iii. The maximum occupancy study performed as part of Environmental Monitoring Process Qualification (EMPQ) of (b) (4) area is inadequate. For example,

a. It did not challenge maximum occupancy of (b) (4)

b. Maximum occupancy of production rooms was not always challenged throughout the duration of environmental sample collection. For example, in Grade C (b) (4) (b) (4) room (b) (4) (recommended maximum occupancy (b) (4) only (b) (4) operators were present for (b) (4) of (b) (4) viable sample collection on 31 May 2024 (b) (4) of the study).

c. You do not have sufficient data to support increased number of personnel allowed (b) (4) (b) (4) in most of production rooms. For example, up to (b) (4) personnel are allowed in Grade D (b) (4) room (b) (4) but only (b) (4) EMPQ run supporting this occupancy was performed.

iv. During gowning for entry into Grade C rooms of the (b) (4) and (b) (4) areas, shoe covers are replaced leaving (b) (4) shoes exposed in Grade D/Grade C (b) (4) Similarly, bare skin is exposed in (b) (4) Grade D (b) (4) as gloves are replaced upon crossing to Grade D side of the (b) (4)

C. The routine environmental monitoring (EM) program at the facility is not optimized for detection of environmental contaminants and monitoring the state of the environmental control. For example,

i. A limited number of worst-case locations are included in the EM program. Floor viable surface sampling in all classified areas of (b) (4) is limited to (b) (4) sampling points: (b) (4) (b) (4)

ii. You did not establish contamination recovery rate limits for EM trending in Grade C areas of the DP facility and collect this data for information only. Additionally, recovery rates are (b) (4) for different sampling methods, potentially masking significant trends.

D. Your firm lacks an established cleaning and sanitization program to prevent the introduction of microbial contamination into controlled sterile DP manufacturing environment. In particular,

i. The disinfectant efficacy study does not support the intended use of the cleaning reagents as it was not performed at the end of the assigned post-opening expiry date of disinfectants. Additionally, efficacy of all disinfectants used in the facility, with the exception of (b) (4) was evaluated in conjunction with removing bacteria from (b) (4) using mechanical action (wipe).

ii. Your SOP-1911 ver. 16, effective 28 Jun 2025, implemented a requirement for maintaining (b) (4) contact time and reapplication of disinfectants for Grade A and B areas only. For all other classified areas of the facility (b) (4) contact time established by your disinfectant efficacy studies is not maintained.

iii. During tour of the (b) (4) and (b) (4) areas of the facility on June 26, 2024 floors of the classified areas were observed sticky throughout. Standing water under (b) (4) tank in (b) (4) area and pieces of debris were also observed on the floors of (b) (4) and Grade D areas.

iii. On 01 Jul 2025 a piece of clean room wipe was observed on the floor of Grade C (b) (4) room (b) (4) during setup for bulk DS filling operations. The wipes were used during the (b) (4) following which Level 1 cleaning of the room and associated (b) (4) was performed from (b) (4) (b) (4) a total of (b) (4) The cleaning consisted of disinfection of all high frequency touch point surfaces and the floors, including temporary movement of equipment to ensure full floor coverage required per SOP-1911 ver.16.

v. Cleanability of the classified areas cannot always be ensured. For example, on 01 Jul 2025 Grade C (b) (4) was observed crowded with (b) (4) totes used for (b) (4) operation during (b) (4) As the totes contained (b) (4) and cleaners were prohibited from moving them, adequate cleaning of the (b) (4) cannot be assured.

Additionally, benches separating differently classified areas in (b) (4) Grade D and Grade D/C (b) (4) have a low profile impeding effective cleaning under the benches. Your SOP-1911 ver. 16 does not describe cleaning of (b) (4)

vi. Your firm failed to conduct appropriate studies demonstrating that cleaning and disinfection processes effectively reduce disinfectant residues to acceptable levels on non-product contact surfaces in your DS and DP manufacturing areas including the RABS filling line.

E. There is a lack of assurance that your cleaning procedures for product-contacting process equipment in your DS manufacturing facilities are effective in preventing cross contamination. For example, your cleaning validation study, REP-4046 (version: 2.0), does not include all surface (swab) samples from all areas that are the hardest to clean, such as the (b) (4) valves from the

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[redacted] (b) (4)

F. You failed to ensure that the [redacted] (b) (4) system was adequately controlled, maintained, and monitored to ensure it consistently produces [redacted] (b) (4) that meets USP monograph with appropriate microbial limits. Various microorganisms known to form biofilm, such as *Ralstonia spp.*, *Rhodotorula spp.*, and *Methylobacterium spp.* were recovered continuously in your [redacted] (b) (4) samples from July 2023, with *Methylobacterium spp.* recoveries observed as recently as 25 Apr 2025. DEV-004789 investigation into recurrent recovery of *Methylobacterium spp.* was closed on 13 June 2025, with six CAPAs pending implementation and effectiveness check at the close out of the inspection on 04 Jul 2025.

Observation 4

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

Specifically,

A. While observing the aseptic setup and filling operations on the [redacted] (b) (4) Filling Line for the manufacture of [redacted] (b) (4) DP product Batch # [redacted] (b) (4) (on 01JUL2025) and [redacted] (b) (4) DP Batch # [redacted] (b) (4) (on 27 JUN 2025), the following deficiencies in the aseptic processes were noted:

   i. During the [redacted] (b) (4) process, the [redacted] (b) (4) portion of the [redacted] (b) (4) unit disrupted the first air above the exposed [redacted] (b) (4). Subsequently, the [redacted] (b) (4) laminar airflow units within the Restricted Access Barrier System (RABS).

   ii. During installation of the filling and stoppering stations, the operator was observed handling unprotected sterile parts, including [redacted] (b) (4) collection hoses, and [redacted] (b) (4) with his gloved hands. These components are positioned directly above the exposed [redacted] (b) (4) and product during the filling and stoppering process.

   iii. During [redacted] (b) (4) tube installation, the operator's gloved hand and non-sterile [redacted] (b) (4) disrupted the first air over the exposed tube.

B. Your [redacted] (b) (4) visual inspection program does not provide adequate assurance that finished products manufactured at your facility possess their purported quality attributes. Specifically, [redacted] (b) (4) containing foreign matter or particles in [redacted] (b) (4) are not classified as critical defects, despite their potential to compromise container integrity and to create a risk of microbial contamination of the sterile product.

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C. Aseptic personnel qualification does not require inclusion of all critical interventions during aseptic process simulation (media fill). Currently, (b) (4) aseptic operators are certified for Grade A interventions. No evaluation was conducted to verify that each certified operator had performed all routine and corrective critical interventions, including the complete aseptic set-up processes of filling and stoppering parts, during aseptic process simulation.

D. Your firm lacks adequate assurance that critical process equipment used for sterile drug product manufacturing is maintained in a validated state. For example, the (b) (4) Line (b) (4) (b) (4) used for sterilizing drug product filling and stoppering components does not have proper validation or routine revalidation for (b) (4) sterilization.

Observation 5

Written records of unexplained discrepancies or the failure of a batch or any of its components to meet specification, do not always contain a thorough investigation, or appropriate documentation, conclusions, and follow-up.

Specifically,

A. You implemented a QMS update for management of OOS/OOE events and associated manufacturing investigations under one laboratory investigation (LI-xxxx) record on 10 Jul 2024. As a result, in deviation from your *SOP-0922 v.18*, deviation records (DEV-xxxx) are no longer opened for unplanned departures from specification, acceptance criteria or other conformance standards confirmed by your initial laboratory investigation. Manufacturing investigations associated with laboratory investigations were not included in your (b) (4) deviation trending.

B. Your *SOP-0922 v. 18* provides for cancellation of deviations, with assessment and documentation of justification by your Quality Unit (QU). From 01 Apr 2023 (47) deviations were cancelled. For example:

   i. DEV-3197 opened 10 Aug 2023 for failure of (b) (4) to (b) (4) proceed to (b) (4) (b) (4) during manufacture of (b) (4) batch (b) (4) due to incorrect (b) (4) installation was cancelled without further investigation and CAPA implementation based on lack of product and process impact and due to being a "one time event… corrected immediately in the same batch".

   ii. DEV-4246 opened 11 Oct 2024 for (b) (4) CFU of suspected *Bacillus spp.* recovered in Grade B (b) (4) air monitoring), DEV-4308 opened 05 Nov 2024 for (b) (4) CFU of suspected *Bacillus spp.* recovered from personnel monitoring, DEV-4754 opened 22 Apr 2025 for (b) (4) CFU of suspected

Bacillus spp. in Grade B (b) (4) air monitoring). In all cases another objectionable organism, *Pseudomonas spp.*, was identified and these deviations were cancelled.

iii. DEV-3189 opened 01 Aug 2023 for failure to remeasure (b) (4) in-process endotoxin sample within the required sample hold time of (b) (4) The deviation was cancelled with a conclusion that the sample hold time was applicable to the initial measurement only and the deviation was raised in error. There is no data to support absence of endotoxin masking in the samples held for over (b) (4)

C. Your SOP-0922 v.18 provides for managing minor departures from GMP/GDP as quality incidents (QI-xxxx or EVxxxx-xxx prior to 01 Dec 2024). Such incidents are not always fully investigated and remediated as root cause is deemed obvious. For example,

i. From 10 July 2024 you opened 17 quality incidents and events involving failure to review various logbooks within the required timeframe. Although CAPAs were implemented in response to some of these events, they failed to prevent their reoccurrence.

ii. Several quality incidents related to data integrity and document control (e.g., QI-000001 opened on 03 Dec 2024 for operator using "calibration" login, QI-000088 opened 12 Feb 2025 for QA issuing controlled document without required header and footer) were closed by QA without further investigation.

iii. Several quality incidents were closed with QA requirement for further investigation: QI-000064 opened 28 Jan 2025 (temperature excursion in (b) (4) room), QI-000071 opened 03 Feb 2025 (deviation from (b) (4) requirements), and QI-000107 opened 21 Feb 2025 (late entry performed in MBR). There is no evidence that a follow-up deviation investigation was performed for any of these quality incidents.

vi. QI-000106 opened 21 Feb 2025 for use of a different (b) (4) probe communication cable due to the correct cable unavailability. The event required automation changes to prevent alarms from blocking the (b) (4) initiation. The incident was closed without investigation to be managed under a temporary change control.

These events represent departures from GMP requirements and therefore do not meet your definition of quality incidents in SOP-0922 v.17 effective at the time of their opening.

D. There is no assurance that the deviation recurrence check required as part of your investigation of deviations and quality incidents per *SOP-0922 v. 18* is complete. Specifically,

i. Deviation recurrence check performed for LI-xxxx, DEV-xxxx, QI-xxxx records is limited to their

respective pool and does not include similar deviations opened as a different type of record.

ii. The QMS recurrence check functionality used prior to (b) (4) failed to identify cancelled DEV-3417 for pipette calibration failure opened (b) (4) and closed (b) (4) when performing recurrence check for the previous (b) (4) associated with DEV-3839 for QC pipette calibration failure opened on (b) (4) There is no evidence that cancelled deviations are not being masked from recurrence check performed by the current QMS version.

iii. You did not perform recurrence check for QI-xxxx records opened prior to 24 Jun 2025, when SOP-0922 v.18 requiring opening a deviation if a quality incident occurs (b) (4) times within a (b) (4) (b) (4) period was approved. No retrospective review of QI-xxxx records was performed.

G. Critical deviations are not always classified as such. For example, critical DEV-003917 opened on 17 Apr 2024 for (b) (4) TruBio DeltaV system alarms and events data loss was categorized as major.

H. During the (b) (4) performance qualification of the (b) (4) system in (b) (4) testing failed to meet predetermined acceptance criteria in (b) (4) of (b) (4) procedural steps. For the (b) (4) deficiencies that occurred during the (b) (4) step and (b) (4) step, your firm failed to conduct adequate investigation or provide scientific justification regarding the acceptability of the equipment performance.

Additionally, recurring (b) (4) process issues have been observed with the (b) (4) system. During the performance qualification discrepancy investigation, (b) (4) process issues were identified as the cause of (b) (4) performance in the (b) (4) step. Between (b) (4) and (b) (4) five deviation reports (DEV-003494, DEV-003495, DEV-003558, DEV-003559, and DEV-003645) were opened due to (b) (4) process issues with the (b) (4) system.

Observation 6

Laboratory controls do not include the establishment of scientifically sound and appropriate standards designed to assure that components and in-process materials conform to appropriate standards of identity, strength, quality, and purity.

Specifically,

A. Duplicates within the (b) (4) series (reference, control, or test samples) are removed from potency data analysis for (b) (4) when exceeding the system suitability criteria for percent coefficient of variation (CV), without sound scientific justification.

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B. Current procedures for managing critical QC reagents are inadequate. Specifically, [(b) (4)] inventory checks are performed for primary and working reference standards for [(b) (4)] [(b) (4)] by directly placing them at room temperature, which may lead to inadvertent thawing that could impact the stability of these critical reagents.

C. An out of specification (OOS) result was reported under LI-001187 for potency testing of [(b) (4)] drug product. While the initial lab investigation did not identify obvious errors, the OOS investigation was closed without conducting a thorough root cause analysis or providing adequate justification, prior to repeat testing.

D. A confirmed OOS result (OOS – 0144) was observed for subvisible particles > [(b) (4)] µm exceeding USP [(b) (4)] limits during fill homogeneity testing and no assignable cause was found. This OOS was linked to the beginning of the fill. The batch was released based upon acceptable release testing results, and due to no variations to the process. QC testing evaluates [(b) (4)] vials from the [(b) (4)] filling process. This investigation was inadequate because that did not include enhanced testing for subvisible particles of potentially impacted [(b) (4)] from the [(b) (4)] of the fill.

Observation 7

Your firm's documentation practices are deficient.

Specifically,

A. During batch record review, I (LB) noted that an unexecuted manufacturing step was signed as performed by the operator and verified by second person as having been observed (Step [(b) (4)] of [(b) (4)] A lack of good documentation practices is also evidenced by at least thirty-five (35) deviations related to incomplete documentation and missing second person verification, dating from Sep 2023 (major DEV-003274) to Jun 2025 (e.g., DEV-004933 and QI-000337). Your firm failed to implement an adequate and effective CAPA to address the recurring poor documentation practices.

B. The filter integrity testing records for High-Efficiency Particulate Air (HEPA) filters installed in the classified manufacturing areas and those installed in the [(b) (4)] Filling Line are deficient in that they do not include complete records of the testing data. Specifically, the measured leakage (penetration) value(s) for each test is (are) not documented to ensure an appropriate investigation in the event of an HEPA filter integrity test failure. Your current documentation practice does not adequately ensure the accuracy and completeness of data.

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C. Your firm failed to implement appropriate access control over GMP records. For example,

i. During a tour of QA area on 01 July 2025, controlled QC records and two QC label printers were found in an unsecure location where they could be accessed by anyone with the main building access. Additionally, keys to access GMP documents that are under review by QA or placed into the archive are kept in lockboxes with a numeric code access. Although some of these lockboxes are located within the general access area, the codes are not periodically changed and there is no system in place for lockbox access traceability.

ii. During tour of the QA office responsible for issuing batch records on 01 July 2025, the door to the office was observed open. The office is used for printing and storage of batch records and the colored batch record paper.

iii. Controlled documents are accessible to operators and analysts in the Veeva electronic system and can be printed by unauthorized personnel, as evidenced by: DEV-003418 which occurred on 03NOV2023, DEV-003513 which occurred 22Nov2023, DEV-003732 which occurred 01Dec2023, and EV2024-056 which occurred 27Sep2024. This was also demonstrated by a SME by logging onto the Veeva system during this inspection. Your firm failed to implement adequate CAPAs to ensure proper control over access to controlled GMP documents.

iv. Management of superseded versions of controlled documents and standard operating procedures (SOPs) is inadequate. Superseded versions of controlled manufacturing batch record (MBR) and manufacturing laboratory records (MLR) were printed for use, as evidenced by EV2024-077 (occurred on 27NOV2024), QI-000331 (occurred 25MAR2025). In addition, superseded versions of SOPs can be printed by SMEs from Veeva system as demonstrated.

D. Master Batch Record (MBR) Instructions are inadequate or unclear. For example,

i. Steps (b) (4) and (b) (4) of the (b) (4) step of the (b) (4) MBR (b) (4) and Steps (b) (4) and of the MBR (b) (4) provide instructions to acknowledge (b) (4) however they do not capture or limit the (b) (4) is a known vulnerability for (b) (4) and the (b) (4) should be maintained consistent with those supported by (b) (4) studies.

ii. Refer to Steps (b) (4) and (b) (4) of the (b) (4) step of the (b) (4) MBR (b) (4) for (b) (4) of (b) (4) which provide instructions for actions to be taken in the event of (b) (4) These steps do not include instruction on specifically how much to (b) (4) or a precise description of the trigger to replace a (b) (4)

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		Ekaterina Allen, PhD, Pharmaceutical Scientist Leiyun Boone, PhD, Lead Biologist Kathryn King, PhD, Biologist Hyung-yul Lee, Ph.D, Pharmaceutical Scientist Della Shin, PhD, Pharmaceutical Scientist Zhong Li, Ph.D., Senior Regulatory Specialist	July 4, 2025

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
CDER/OPQ/OPMA 10903 New Hampshire Avenue; White Oak Building 51/Room 2269 Silver Spring, MD 20993-0002 E-mail: OPMABLAInspection483Responses@fda.hhs.gov	06/26/2025 -07/04/2025
	FEI NUMBER 3013702557

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Mr. Robert Wessman, CEO	
FIRM NAME Alvotech HF.	STREET ADDRESS Saemundargata 15-19
CITY, STATE, ZIP CODE, COUNTRY Reykjavik, 102, Iceland	TYPE ESTABLISHMENT INSPECTED Drug Substance and Drug Product Manufacturer

iii. The calculation of (b) (4) a critical process parameter, is incorrect in the batch records. The calculation for (b) (4) in production (b) (4) is based on the (b) (4) rather than the (b) (4)

Observation 8

Your firm failed to exercise appropriate controls to protect the electronic data acquisition and process control systems used for DS and DP manufacturing and testing.

Specifically,

A. Unique login identifications for each user have not been established for computerized systems. For example, your staff used a shared username and password to log into a laptop (b) (4) to access the (b) (4) data acquisition system for (b) (4) of critical process equipment, including (b) (4) validation.

B. Your firm's QA electronic data review process is deficient. For example, audit trails enabled in the (b) (4) data acquisition systems are not reviewed for each data set during the (b) (4) (b) (4) review processes. In addition, during data review only final printouts of the measured results are reviewed and they are not verified against the original electronic records.

C. During the power outage in January 2024, the (b) (4) TruBio DeltaV system was severely impacted when the DeltaV Professional PLUS server could not be restarted and required rebuilding with database restoration. A revalidation of the computerized system was not performed after the system was restored.

Observation 9

Your quality unit does not fully exercise its responsibilities regarding service contractor qualification.

Specifically,

A. Your quality unit has not conducted on-site GMP audits of all contractor service providers who perform critical qualification and validation activities at your DS and DP manufacturing facility. For example, no audits have been conducted of the following providers:

i. (b) (4) provider of qualification activities for the HVAC system (including HEPA filters), Unidirectional Air Flow (LAF) units, and Microbiological Safety Cabinets.

ii. (b) (4) provider of validator test systems for (b) (4)

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B. You contracted (b) (4) to perform cleaning of Grade C and D areas. Although (b) (4) were approved by QA for cleaning in September 2020, you did not have a quality agreement in place until 23 Jun 2025. The current agreement fulfills your requirement for the services deemed to have low impact. Additionally, you did not ensure that training of (b) (4) employees includes basic GMP training.

Observation 10

Materials management is deficient.

Specifically,

A. Management of raw materials is inadequate. Not all raw materials are tested for identity by the firm prior to release for use. Based on the lists provided during this inspection, a total of (b) (4) (b) (4) raw materials are released solely based on certificate of analysis (CoA).

B. There is a lack of documentation for disposal of contaminated (b) (4) lot (b) (4) which was used in the production of (b) (4) batch (b) (4) was subsequently determined to be contaminated based on DEV-003479. The firm stated that the contaminated (b) (4) was discarded; however, no supporting documentation could be located to verify the final disposal of this material.

C. DS was shipped in a container closure not validated for the intended use, as evidenced by damage to DS bags following shipment to a CMO (b) (4) These shipments utilized SOP-1483, v3.0, which did not include instruction for shipment of DS. Damage to the storage bags, if unnoticed, is a safety risk for patients.

EA 04 JUL 2025

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