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	09/09/2024-09/17/2024
	FEI NUMBER: 3013702557

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

FIRM NAME	STREET ADDRESS
Alvotech HF	Saemundargotu 15-19
CITY, STATE, ZIP CODE, COUNTRY: Reykjavik, 102, Iceland	TYPE ESTABLISHMENT INSPECTED: Biological Drug Substance/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

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

A. Your Quality Unit failed to implement adequate and reliable controls for ensuring that distributed (b) (4) (b) (4) mg/ (b) (4) mL (b) (4) drug product, (b) (4) or any of its components always comply with the quality they represent to possess

Specifically, nine (9) complaints (No-USA distributed lots) related to (b) (4) mg (b) (4) mL (b) (4) drug product were investigated between March 2023 and August 2024, reporting issues with the (b) (4) (b) (4)

Complaint Number	Closing Date	Description of the event
COM-009	10-Mar-23	(b) (4)
COM-024	03-Mar-23	
COM-025	03-Mar-23	
COM-026	01-Jun-23	
COM-062	01-Nov-23	
COM-086	10-Nov-23	
COM-115	15-Jan-24	

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Jose E Melendez, Investigator	September 17,2024

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COM-154	26-May-24	(b) (4)
COMP-001048	28-Aug-24	

The complaint investigations identified "(b) (4)" as the root cause for the reported event. Per your Quality Unit "(b) (4)".

Your Quality Unit continues to release batches of (b) (4) ng (b) (4) mL, based on the risk assessment REP-4641 (Risk Assessment Report for the (b) (4) Issue) that concluded that "*a (b) (4) will not cause a significant harm to patients*".

B. Your Quality Unit did not submit a Biological Product Deviation Report (BPDR) for the "(b) (4)" defect identified in the (b) (4) in (b) (4) mg (b) (4) mL drug product (b) (4).

According to your assessment, this defect could cause the (b) (4) of the drug (b) (4) (b) (4) meaning that since the (b) (4) does not perform as expected, the patient cannot administer the drug.

OBSERVATION 2

Your firm failed to thoroughly investigate any unexplained discrepancy or failure of a batch or any of its components to meet any of its specifications, whether or not the batch has already been distributed.

From January 2022 to August 2024, your Quality Control (QC) laboratory invalidated approximately (b) (4) endotoxin tests for (b) (4) (i.e., (b) (4) in-process (i.e., (b) (4) and drug substance/product samples. The out-of-specification results are associated to failures in spike recovery, sample Coefficient of Variation (CV) and spike CV).

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Your quality control laboratory has attributed the out-of-specifications (OOS) results to a combination of factors such as analysts' error, pipette contamination, and cartridges with "hot wells," among others.

According to your assessment, "hot wells" is defined as one (1) sample channel of the cartridge reacting within the range of the curve (suggests endotoxin is present), and one (1) channel does not react (suggests no endotoxin presence). Additionally, "hot wells" shows variability in the CV producing OOS results.

In those events where OOS results were invalidated due to pipetting error or sample contamination, your investigation does not include conclusive evidence to support the justification for invalidation. Additionally, it is unclear whether a corrective action was implemented.

Regarding cartridges with "hot wells", your Quality Unit has not worked in continuing collaboration with the cartridge supplier to ensure that quality commitments and reliability of the endotoxin test are met.

09/17/2024

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