DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
555 Winderley Place, Suite 200 Maitland, FL 32751 (407)475-4700 Fax:(407)475-4768	12/3/2024-12/11/2024* FEI NUMBER 1000525461

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Adam S. Grossman, President & CEO

FIRM NAME	STREET ADDRESS
ADMA Biologics, Inc	5800 Pk Commrce Blvd
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Boca Raton, FL 33487-8222	Licensed Biological Drug 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

There is a failure to thoroughly review any unexplained discrepancy whether or not the batch has been already distributed.

Specifically,

a. You initiated deviation DEV23041 on March 28, 2023, when (b) (4) of stoppers with vials was observed during the filling process of Bivigam lot 233798. To address the (b) (4), you decided to discontinue the fill and initiate repairs. The bulk line was (b) (4), and the bulk was (b) (4) the fill (b) (4). You stated that the unfilled bulk was returned to refrigerated storage and "was successfully reprocessed as Bivigam Fill Lot 234608 on 03/29/2023." There was no further investigation into potential impact of (b) (4) on the bulk. In addition, there is no approved procedure for (b) (4) of Bivigam bulk, and the currently approved license includes no provision for reprocessing or reworking of Bivigam. Bivigam fill lot 234608 was released to the US market on 09/05/23. Additional examples of (b) (4) after stopped Bivigam (b) (4) filling operations are presented in the table below. Each Bivigam lot was released to the US market.

Deviation ID	Date	Original Batch ID	Description	New Batch ID / Release date

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EMPLOYEE(S) SIGNATURE
Thai D Truong, Investigator
Burnell M Henry, Investigator
Jennifer L Reed, FDA Center Employee

X Thai D Truong Investigator Signed By: 0014274389 Date Signed: 12-11-2024 08:16:29

DATE ISSUED
12/11/2024

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DEV21150	10/27/21	Bivigam (b) (4)	Scratched vials required fill stop for repair	(b) (4)
DEV21106	08/04/21	Bivigam 228257	Calibration error required fill stop	228257-1 / 07/20/22
DEV21148	10/19/21	Bivigam 228663	Calibration error required fill stop	228663-1 / 09/09/22
DEV23058	04/26/23	Bivigam 233803	Recalibration of (b)(4) error required fill stop	234896 09/28/23

b. On November 13, 2024, you received a (b) (4) notification from ADMA BioCenters Georgia regarding (b) (4) HIV NAT positive plasma units which had been inadvertently shipped to your manufacturing facility. You received confirmation for the HIV NAT positive status of the units on November 21, 2024. In follow-up to the initial report, you identified two Bivigam fill lots, 309923 and 310023, which had been manufactured from plasma pools which included the (b) (4) units. Your risk assessment after receipt of the (b) (4) notification was deficient. For example, there was no specific re-evaluation of pathogen (b) (4) to assure no excursions or deviations had occurred during manufacture. There was no estimation of (b) (4) pathogen (b) (4) in the affected batches, and no comparison of pathogen (b) (4) with theoretical limits for pathogen (b) (4) in the (b) (4). It was also noted that manufacture of Bivigam with (b) (4) plasma units qualifies as an

unexpected event that may affect the safety, purity, or potency of the product; however, no BPDR was submitted for Bivigam lots 309923 and 310023, both of which were released to the US market.

c. You opened deviation DEV21126 on September 15, 2021, after unexpectedly (b) (4) was observed during bulk filtration of Bivigam lot (b) (4). Filtration was stopped just before the 90 (b) (4), and both filtered and unfiltered bulk were moved to (b) (4). After a series of experiments on (b) (4) samples, you noted excess (b) (4), and hypothesized that failure of (b) (4) by the (b) (4) was the root cause for (b) (4) of the bulk filter. Nevertheless, this root cause was not followed up and no further investigation or CAPAs were undertaken related to failure of (b) (4) removal. The lot was released to the US market.

OBSERVATION 2

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

Specifically,

a. Particle levels were not adequately monitored or well-controlled in the Grade (b) (4) (ISO (b) (4)) (b) (4) filling (b) (4) in which sterile drug components are exposed during filling operations. For example:

I. Particulates from filling components used during the aseptic filling operation were found in your post filled drug product vials. Since August 2021, you have initiated more than ten deviations for particulates that (b) (4) action limit, and about (b) (4) events for particulates (b) (4) alert limits for (b) (4) particulates found inside (b) (4) filled drug product vials.

II. A probe used to measure total non-viable particulates in the Grade (b) (4) (ISO (b) (4)) (b) (4)

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Filling (b) (4) is not placed in (b) (4) to the aseptic filling. Instead, the probe was observed to be placed (b) (4) the vial (b) (4) .

b. There was a lack of information about the microbial quality of the environment in which aseptic processing is performed. For example:

I. There is no monitoring of the air for microorganisms during aseptic filling and stoppering (capping) operations for your drug products.

II. You classified your (b) (4) filling (b) (4) as Grade (b) (4) (ISO (b) (4)), however, your routine environmental monitoring only performed to meet Grade (b) (4) (ISO (b) (4)) classification.

OBSERVATION 3

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

Specifically,

You currently monitor temperature, humidity, air pressure differential, and non-viable particulates during filling operation in your Grade (b) (4) (ISO (b) (4)) environment. You failed to establish a procedure on how to handle and respond to an excursion when acceptable limits are exceeded during filling operations.

***DATES OF INSPECTION**

12/03/2024(Tue), 12/04/2024(Wed), 12/05/2024(Thu), 12/06/2024(Fri), 12/09/2024(Mon), 12/10/2024(Tue), 12/11/2024(Wed)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Thai D Truong, Investigator Burnell M Henry, Investigator Jennifer L Reed, FDA Center Employee	X Thai D Truong Investigator Signed By: 0014274389 Date Signed: 12-11-2024 08:16:29	12/11/2024

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X Jennifer L Reed
FDA Center Employee
Signed By: Jennifer L. Reed -S
Date Signed: 12-11-2024 08:17:30

X Burnell M Henry
Investigator
Signed By: Burnell M. Henry -S
Date Signed: 12-11-2024 08:24:06

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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."