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	03/04/2025-03/11/2025
	FEI NUMBER 3011948449

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Keita Hirabayashi, Site Head	
FIRM NAME Fujifilm Diosynth Biotechnologies Texas, LLC	STREET ADDRESS 3939 Fujifilm Way
CITY, STATE, ZIP CODE, COUNTRY College Station, TX, 77845, 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 FIRMWE OBSERVED:

Observation 1

Your multi-product manufacturing areas are not adequately controlled to prevent potential cross-contamination. Specifically,

a. There are no physical or procedural segregation controls for materials, equipment, and personnel movements between upstream and downstream manufacturing areas.

b. The clean room grade (CRG) areas lack specified pressure differentials between upstream and downstream manufacturing suites for (b) (4) intermediate, and parameters for air exchange rates for the CRG manufacturing suites have not been defined.

c. There are no established standard operating procedures (SOPs) for managing shared processing areas for concurrent multi-product manufacturing operations.

d. During inspection, it was observed that operators in the CRG and Grade C manufacturing suites frequently left (b) (4) open for extended periods without covers. This issue occurred multiple times during the connection of aseptic (b) (4) to (b) (4) on (b) (4) and (b) (4) Additionally, operators were seen working in the Grade C (b) (4) area without masks while performing these open operations. Operators were also observed spraying (b) (4) for (b) (4) sanitization near open (b) (4) posing risk of (b) (4) contamination to the (b) (4) There are no procedures in place to mitigate potential contamination risks associated with these transient open operations in the CRG and Grade C multi-product environments.

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Observation 2

Your QC laboratory controls used for in-process, release, and stability testing of (b) (4) intermediate do not include appropriate test procedures that assure conformance to appropriate standards of quality and purity. Specifically, the (b) (4) method for in-process testing of (b) (4) intermediate (b) (4) is not adequately verified or validated for its intended use. You reported that between (b) (4) and (b) (4) % (b) (4) out of (b) (4) tests) of (b) (4) tests were invalidated mainly due to failed system suitability criteria resulting from low % recovery of the lowest standard concentration. The lowest standard concentration for this method is also the limit of quantitation (LOQ) for the method, and is therefore, expected to have sufficient recovery. The recurring system suitability failures indicate that there is no assurance that the method is adequately validated and capable of consistently meeting system suitability criteria.

Observation 3

The stability program SOP "FDBT-SOP-0405 (revision 10)" is not being followed. The SOP requires that stability testing for internal tests be initiated within the test initiation windows indicated in Table 2 of Section 4.4.5.5. However, review of historical (b) (4) intermediate stability sample pulling and testing schedules from January 2024 to March 2025 showed that the following stability tests were performed outside of the testing initiation windows specified in the SOP: CEX-HPLC analysis of lot (b) (4) (-20°C, 24-month time-point) performed 78 days past the testing window, lot (b) (4) (-20°C, 24-month time-point) performed 92 days past the testing window, lot (b) (4) (-20°C, 24-month time-point) performed 107 days past the testing window, lot (b) (4) (-20°C and 5°C, 6-month time-point) performed 57 days past the testing window, (b) (4) (-20°C and 5°C, 9-month time-point) performed 24 days past the testing window; and SE-HPLC analysis of lot (b) (4) (-20°C and 5°C, 6-month time-point) performed 29 days past the testing window.

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Observation 4

Your cleaning and sanitization program is deficient in preventing potential contamination in the controlled drug substance manufacturing areas. Specifically,

a. The SOPs (FDBT-SOP-0682, revision 10; FDBT-WI-0040, revision 12; FDBT-WI-0347, revision 3) for Grade A (b) (4) operation and cleaning are inadequate in providing explicit instructions on post-use cleaning. It was observed that only the outer surfaces of the (b) (4) used to hold WCB vials and the cell viability sample cups were cleaned with (b) (4) wipes. However, the areas inside the (b) (4) which had direct contact with vials and cups, were not cleaned post-use.

b. Your cleaning and sanitization procedure for the manufacturing areas in the (b) (4) facility (SOP-0322, revision 21.0) does not require documentation and verification in the cleaning logbooks during the facility cleaning and sanitization that the treated surfaces are wetted and remain wetted for the contact time validated in the disinfectant efficacy studies.

c. Your disinfectant efficacy study (Report # 22-137DET, approved 24 Jan 2023) does not adequately support the sanitization procedure for the antimicrobial and sporicidal effectiveness of the disinfectants and sporicidal agents on all representative manufacturing surfaces in the (b) (4) facility. For example, materials used for (b) (4) (b) (4) computer keyboard, and chairs were not included in the study.

Observation 5

Environmental monitoring (EM) of classified processing areas in your (b) (4) facility for the (b) (4) intermediate manufacturing operations is deficient. Specifically,

a. During the routine EM monitoring of the solution preparation activity room (b) (4) on March 06, 2025, a QC analyst was observed using inadequate sampling technique as the (b) (4) plate did not make full contact with the surfaces while the viable samples were collected.

b. There is no EM sampling for the (b) (4) at the end of WCB vial thaw and inoculation operation.

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Observation 6

Your firm failed to exercise appropriate controls for the electronic data acquisition systems used for (b) (4) intermediate manufacturing. Specifically,

a. There is a lack of documented evidence that the (b) (4) systems and the (b) (4) (b) (4) system have been validated to protect original electronic records and relevant metadata (*e.g.*, audit trails). These systems are utilized to collect and process data from data loggers during the (b) (4) validation of critical process equipment and systems at your facility, including (b) (4) (b) (4) In addition, audit trail review is not performed for each dataset during the validation review. During data review, only final printouts of the measurement results are reviewed, and they are not verified against the original electronic records.

b. Your firm lacks an adequate program for comprehensive evaluation of the (b) (4) system audit trails to identify and address any aberrant trends associated with user-aborted (b) (4) sequences/injections/sample-sets events. Specifically, your firm's dataset audit trail reviews failed to include in-process testing results and "Trial Injections" datasets. System audit trail reviews are only performed (b) (4) In addition, user privilege settings in (b) (4) allow your QC analysts to perform batch processing or manual processing for unsaved live data that they are working with in the Review window before the peak integration is completed and finalized.

Observation 7

SOPs or work instructions are not followed or are inadequate. Specifically,

a. The instructions in the QC release and stability test methods are deficient to ensure conformance to appropriate standards of quality and purity. For example,

   i. FDBT-TM-0226: (b) (4) Analysis of (b) (4) (revision 7). The (b) (4) method is used for in-process, release, and stability testing. There are specific sections of FDBT-TM-0226 that provide instructions

for release testing or in-process testing, but there are no sections that provide instructions for stability testing. In addition: the volume of standard, samples, and (b) (4) (b) (4) solution to be transferred to the vial is not specified; it is not clear if (b) (4) (b) (4) is performed prior to the actual tests or as part of the actual tests, and if the (b) (4) is required to be (b) (4) prior to the (b) (4) runs; the conditions under which a (b) (4) step may be added to (b) (4) of the sample set are not specified; the SOP states that a (b) (4) method must be set up (b) (4) but the procedure for setting up the (b) (4) method is not defined in the SOP; reference to an example (b) (4) that may be used to determine adequacy of the (b) (4) (b) (4) is not provided.

ii. FDBT-TM-0227: (b) (4) Analysis of (b) (4) by (b) (4) Test Method (revision 8): The (b) (4) method is intended for both release and stability testing. There are specific sections of FDBT-TM-0227 that provide instructions for release testing, but there are no sections that provide instructions for stability testing. In addition: the volume of standard, samples, and (b) (4) solution to be transferred to the vial is not specified; the situations under which (b) (4) may be required are not specified; the conditions under which a (b) (4) step may be added to (b) (4) of the sample set are not specified; the SOP states that a (b) (4) method must be set up (b) (4) (b) (4) but the procedure for setting up the (b) (4) method is not defined in the SOP (b) (4) is not specified; references to example (b) (4) that may be used to determine if the (b) (4) of (b) (4) (b) (4) is adequate, and that the (b) (4) profile and (b) (4) of the standard and samples are comparable to those of the reference (b) (4) are not provided.

iii. FDBT-TM-0228: (b) (4) Analysis of (b) (4) (revision 3). The (b) (4) method is used for in-process, release, and stability testing. There are specific sections of FDBT-TM-0228 that provide instructions for release testing or in-process testing, but there are no sections that provide instructions for stability testing. In addition: the volume of each

preparation to be transferred to the (b) (4) µL micro vials is not specified; reference to an example (b) (4) that may be used to determine the presence of the (b) (4) is not provided.

iv. FDBT-TM-0229: (b) (4) Analysis of (b) (4) (revision 4). The volume of each preparation to be transferred to the (b) (4) µL micro vials is not specified. In addition, reference to an example (b) (4) that may be used to determine the presence of the (b) (4) is not provided.

b. The component test to verify the functionality of the (b) (4) (refer to Section 4.7.9 of FDBT-SOP-0192, revision 13) is deficient. Specifically, the (b) (4) acceptance interval for the (b) (4) is set as (b) (4) o (b) (4) which lacks sufficient discriminating power to differentiate the (b) (4) Consequently, there is a lack of assurance that a significant deviation from the (b) (4) in the supplied (b) (4) which can have adverse impact to the (b) (4) intermediate (b) (4) can be detected during the (b) (4) installation.

c. Your quality unit does not fully exercise its responsibilities regarding the critical service contractor qualification. Specifically, your quality unit has not conducted any on-site audit of (b) (4) that is responsible for equipment calibration and (b) (4) validation, and (b) (4) (b) (4) that provides contract laboratory services including disinfectant efficacy studies. In addition, the reliability of the supplier's certificates of analysis/compliance for integrity test has not been verified for the (b) (4) systems including (b) (4) bags.

Observation 8

The intermediate hold times defined in the (b) (4) intermediate batch records at FDBT are inconsistent with the hold times defined in the (b) (4) Specifically, an intermediate hold time of (b) (4) is specified in the (b) (4) for the (b) (4)

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(b) (4) However, the (b) (4) intermediate batch records at FDBT indicate that these process intermediates may be held for up to (b) (4)

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