

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER

CDER/OPQ/OPMA/DBM, Attn: Derek Smith
10903 New Hampshire Ave, Bldg 51, Rm 4225
Silver Spring, MD 20993
E-mail: OPMABLAInspection483Responses@fda.hhs.gov
Industry Information: www.fda.gov/oc/industry

DATE(S) OF INSPECTION

01/17/2022 - 01/25/2022

FEI NUMBER

3016809519

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Francisco Olivera, Site Director

FIRM NAME

GH Genhelix, S.A.

STREET ADDRESS

Parque Tecnologico de Leon C/ Julia Morros s/n

CITY, STATE AND ZIP CODE

Armunia, Leon, 24009, Spain

TYPE OF ESTABLISHMENT INSPECTED

Drug Substance Manufacturing Facility

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DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

OBSERVATION 1

Equipment used in the manufacture and processing of a drug substance shall be suitably located to facilitate operations for its intended use.

Specifically,

During the inspection, (b) (4) batch (b) (4) for batch (b) (4) failed to meet the well-controlled critical process parameter (WC-CPP) (b) (4) of (b) (4) due to the firm not having (b) (4) units in order to perform the unit operation. The firm opened up deviation 22-016 to investigate the root cause. The deviation investigation is ongoing and the impact on product quality is being assessed.

OBSERVATION 2

Material Management is inadequate.

Specifically, the supplier of critical process equipment (b) (4) that are needed to perform (b) (4) essential unit operations, did not deliver the promised number of (b) (4) in your purchase order in December 2021 and missed several agreed upon delivery dates in January 2022 resulting in deviation 22-016.

OBSERVATION 3

Written records of investigations into unexplained discrepancies do not always include conclusions and follow-up which are adequately justified.

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EMPLOYEE(S) SIGNATURE



EMPLOYEE(S) NAME AND TITLE (Print or Type)

Richard Ledwidge, Senior Biologist
Arsen Karapetyan, Investigator

DATE ISSUED

01/25/2022

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Starting around 02/27/2020, three separate out-of-specification results were observed for (b) (4) test at 12 month long term stability time point for (b) (4) drug substance for lot numbers (b) (4). (b) (4) OOS-20-007, OOS-20-008, and OOS-20-012 were initiated in response to these out-of-specification results. Investigations initiated and performed by your Quality unit in response to out-of-specification test results were not scientifically sound or comprehensive. Specifically, Corrective Action/Preventive Action (CAPA's) as a result of investigations did not appear to address an adequate root cause. Additionally, for OOS-20-012, your firm appears to have confirmed the OOS results during investigative testing from the original sample container, only to invalidate the OOS results without scientific justification by testing from a backup sample container.

OBSERVATION 4

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

Specifically,

A. Investigations do not always include complete data derived from all tests necessary to assure compliance with established specifications and standards. During review of laboratory data, we observed multiple sequences where interrupted sample injections were injected and showed that the sample did not run, instead showing "Data Incomplete". Your firm was not aware that data from these injections are retrievable. Samples injected were not documented to be performed, in order to determine whether the samples injected had any discrepancies or appeared to be out of trend. This discrepancy in your firm's ability to retrieve, review and investigate all electronic raw data is a gap in your Data Integrity system.

B. QC Review of chromatographic and non-chromatographic electronic raw data generated by analysts in the QC laboratory is not adequate. QC technicians responsible for electronic data review do not perform a comprehensive review of all potential electronic data generated for all test items in your stand alone and network softwares.

C. Your firm has identified Research and Development laboratory stand alone equipment as back-up testing equipment for QC analysts. There is no procedure in place to review electronic data on these R&D equipment.

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D. Electronic data from previous years (b) (4) stored in folders on stand alone and network systems are not locked. Analysts are free to start, perform, and save testing in all folders.

E. There is no adequate data integrity program in place to include a statistically sound representative review of electronic data by the Quality Unit for standalone and network systems, to ensure completeness, consistency, and accuracy of all chromatographic and non-chromatographic electronic raw data generated by the Quality Control Laboratory.

OBSERVATION 5

Drug Substance filling is inadequate.

Specifically, we observed drug substance bottles filled at a rate which caused splashing and extensive (b) (4).
(b) (4) The nature of the (b) (4) have not been characterized to date.

OBSERVATION 6

(b) (4) cleaning is inadequate.

Specifically, a discoloration in the (b) (4) was observed during the walk through of the downstream operations. The nature of the discoloration is unknown at this time.

OBSERVATION 7

Cell Bank Storage is inadequate.

Specifically, all master cell bank and working cell bank vials are located in a single location, room (b) (4) in the manufacturing building.

OBSERVATION 8

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Batch record documentation is inadequate.

Specifically

a) The instructions to add antifoam in the production bioreactor are unclear and open to operator interpretation. Anti-foam addition has varied (b) (4) across batches in 2021.

b) The instructions to sequentially add (b) (4) during (b) (4) (b) (4) are unclear and not specified in the batch record.

OBSERVATION 9

Class D area cleaning is inadequate.

Specifically, a (b) (4) area used to move (b) (4) between (b) (4) in the manufacturing facility had debris on the floor.

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