DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857 Industry Information: www.fda.gov/oc/industry	9/11-15/2023 FEI NUMBER 3002806649

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Yuzuru Morino, Executive Officer

FIRM NAME	STREET ADDRESS
Central Glass Co., Ltd.	5253, Oazaokiube
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Ube, Yamaguchi, 755-0001, Japan	API 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 (I) (WE) OBSERVED:

Observation 1
Laboratory Controls are inadequate.

Specifically,

a) The working standards used during release testing of for assay and volatile analogues not always elude peaks for the corresponding volatile analogues . During qualification of your working standards one of the requirements is to verify the presence of all peaks. However, injection of standard lot (b) (4) during analysis of commercial (b) (4) API lots (b) (4) does not contain peaks for all volatile analogues at their respective retention time.

b)Access control to samples that have not been assigned and those for which testing has been completed is not restricted. In addition on 9/11/23 completed samples of released (b) (4) batches (b) (4) were observed on the (b) (4) floor of the QC laboratory stored next to samples that were in process of lots (b) (4) (b) (4). Your firm noted verbally that the completed samples were not discarded because they will be used to qualify analysts, however there was no documentation to support this.

c) Your site does not conduct growth promotion of media used to perform environmental monitoring of the filling room used for (b) (4) API.

d)On 9/11/23 I observed a filled GC vial labeled as "extra" unattended in the laboratory near to GC 23 stand alone equipment, when requested for the origin of the vial and content your site could not establish if the vial contained System Suitability (SST) solution, standard, or samples. Your site explained that they believed the vial was filled with System Suitability solution however, there was no documentation for this.

e) During the update of software and hardware for system GC-24 the number of theoretical plates was not

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	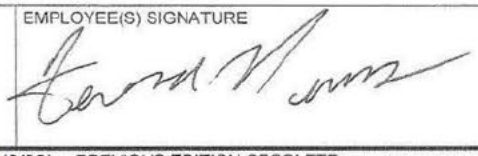	Teresa I. Navas, Investigator	09/15/2023

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calculated prior to placing the system back in use.

Observation 2
Specifications of Water used in the manufacture of APIs do not demonstrate the water is suitable for its intended use.

Specifically, specifications for (b) (4) water and (b) (4) water used for cleaning and processing after (b) (4) (b) (4) do not include testing to confirm the absence of B. Cepacia from your water system.

Observation 3
Your cleaning procedures are not validated.
Specifically,

a)Your firm has not performed validation of the cleaning procedures used to clean equipment that is used for filling API (b) (4) into containers.

b)Procedure #MSE18-33 requires cleaning of manufacturing equipment (b) (4) however the number of consecutive batches manufactured on the equipment in (b) (4) varies. For example the campaign executed to asses the cleaning re-validation study of 10/15/20 consisted of (b) (4) batches, however the previous manufacturing campaign consisted of (b) (4) lots.

c) Cleaning validation studies for bulk containers including clean hold time do not include samples to determine appropriate microbial levels.

d) Removal of (b) (4) used during (b) (4) is verified using (b) (4) this method is not sensitive to indicate if (b) (4) is reduced to levels that indicate it has been removed.

e)Your test method used from 2015-2020 to evaluate cleaning validation samples had an LOQ of (b) (4) ppm but your specifications for residue were (b) (4) ppm. This test was not suitable for the evaluation of cleaning validation samples during this time.

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Observation 4
Changes that could affect the production and control of the intermediate or API are not always handled using the formal change control system.

Specifically,
a) The following changes were not handled using the change control system (list is not exhaustive):

Change of AC system in (b) (4) filling room, your firm noted that the reason to not execute a change control for this change was because the AC was being replaced with a unit that met the same specifications. However at the time of the change the comparison between the old and new unit was not documented to justify the lack of change control.

On 8/6/23 UQSE20-19 test method used to evaluate rinse samples from cleaning validation was changed to obtain a lower LOD and LOQ the residue limit on equipment was also changed from (b) (4) ppm to (b) (4) ppm. The reason for not performing this change using the change control program was not documented.

b) Change control CCQ22-17 enacted to address change in storage of (b) (4) medium used by QC from refrigeration to room temperature states that the firm will verify if the storage conditions change has any impact on tests. However there were no steps, protocol or instructions on how your firm would perform the noted verification. In addition on 9/15/23 I observed that there is no calibrated device to monitor the temperature of the room where the media is stored.

Observation 5
Your validation protocols for the execution of revalidation studies do not specify critical process steps.
Your process validation studies for (b) (4) do not show the critical process parameters that were going to be studied, review of batch records shows that the validation study did not include variation of parameters within the established ranges. In addition parameters such as the timer used to control the flow in the (b) (4) are not defined as critical process parameters.

Observation 6
Your receiving procedures for raw materials are inadequate.

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Specifically,
You do not have procedures that require proof from your vendor that the tanks used to deliver (b) (4) (b) (4) are properly cleaned between each delivery.

9/15/23
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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 judgement, 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."