DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
FDA/CBER/OCBQ/Division of Manufacturing and Product Quality 10903 New Hampshire Avenue, Silver Spring, MD 20993 Attention: Jay Eltermann, Building 71, Room 6038 Telephone: (240) 402-9168 Industry Information: www.fda.gov/oc/industry	06/07/2021 to 06/11/2021
	FEI NUMBER 3019202665

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Jose Oberholzer, MD, President/founder and Chief Medical Officer

FIRM NAME	STREET ADDRESS
CellTrans Islet Isolation facility	1740 W. Taylor street
CITY, STATE AND ZIP CODE Chicago, IL 60612	TYPE OF ESTABLISHMENT INSPECTED cell and gene Therapy manufacture

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

Observation 1

Your firm's Quality Unit lacks a procedure/policy that details requirements for the following:

An (b) (4) is used for receipt of, for example, deliveries of your firm's (b) (4) or (b) (4). There is no procedure or policy in place that addresses the potential for deliveries that may be (b) (4) or (b) (4) or where possible storage in (b) (4) may occur.

Lack of oversight of a sterilization firm:

• Sterilization of CellTrans equipment is not performed according to the validated process. Specifically, it was found that the (b) (4) with CellTrans equipment and other hospital equipment based on (b) (4) and available (b) (4). The (b) (4) validation report only describes load items from CellTrans.

• Sterilization load can be re-sterilized, however only documented final sterilization information is forwarded to CellTrans, initial failed or incomplete runs are not required to be reported to CellTrans as of this inspection.

Observation 2

The current deviation reporting procedure was found deficient, for example:

• During review of the (b) (4) system for monitoring of (b) (4) temperature and humidity, it was found that temperature excursions are not properly documented and reported as deviations.

• (b) (4) HEPA filters were found to have (b) (4) during routine (b) (4) HEPA filter certification. However, there is no documentation that a (b) (4) performed (b) (4) whether the percentage of area (b) (4) was

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Pete (Pankaj) Amin, CSO Gene Arcy, CSO Prajakta Varadkar Biologist	06/11/2021

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within an allowable limit or any impact on room environmental quality.

Observation 3

Final product lots were released with incomplete batch record or failed lot release specifications. The batch records for these lots were part of your BLA submission.

Specifically Lots (b) (4) were released for (b) (4) with incomplete information of purity tests in the batch record. Lot (b) (4) was released for (b) (4) with failed potency test.

Observation 4

Regarding your firm's current aseptic process observed during inspection we noted the following deficiencies:

• Sterile equipment was exposed to ISO (b) (4) before transferring into the (b) (4) (b) (4) (ISO (b) (4)) for use in your firm's aseptic process.

• An (b) (4) over exposed sterile equipment during a process performed within a (b) (4) (ISO (b) (4)).

• A (b) (4) study was not performed for any of the (b) (4) that are used for aseptic processing. (b) (4) study performed for the ISO (b) (4) failed to include (b) (4) conditions.

• Equipment and other items were observed in the (b) (4) partially blocking the ISO (b) (4) (b) (4)

• The ISO (b) (4) contains equipment that are not used for processing that may interfere with room cleaning and impact room quality such as the following: (b) (4) that have not functioned for many years, (b) (4) not used for processing, and (b) (4) on a wall.

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• A pressure differential between rooms of different classifications is not continuously monitored; it is only monitored during (b) (4) and (b) (4) using (b) (4)

Observation 5

Your gowning procedures are deficient. Specifically,

• The SOP, Gowning: Entering and Exiting Procedures for the Islet Isolation Facility, MFG-SOP-201, section 8.1 "Gowning Process: Preparation Step," requires changing from (b) (4) including the (b) (4) as part of the preparation. The (b) (4) include (b) (4) and (b) (4) and (b) (4) There is no assurance that (b) (4) have not been contaminated by the (b) (4) environment. The SOP also requires that (b) (4) be stored in an (b) (4) which is done after (b) (4)

• (b) (4) gowning is necessary to work in ISO (b) (4) environments to perform aseptic manufacturing steps, as per the SOP, Sterile Gowning Technique, MFG-SOP-221. Your firm does not conduct training in, nor have a gowning qualification program for, such sterile gowning of personnel as described by the SOP.

Observation 6

(b) (4) equipment qualification is deficient. Specifically, the qualification was not performed under the conditions of use (b) (4) and the verification of (b) (4) integrity was limited to visual inspection of the (b) (4).

Observation 7

Effectiveness of the (b) (4) used for facility and (b) (4) cleaning was not demonstrated. (b) (4) effectiveness study design did not include acceptance criteria to demonstrate required (b) (4) did not

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specify (b) (4) used or their (b) (4), and (b) (4) is unknown.

Observation 8

CellTrans does not require periodic verification of (b) (4) cleaning used for (b) (4). No such verification has been performed since 2018 when the initial cleaning validation was completed.

Observation 9

The Quality Unit oversight of (b) (4) is deficient. Specifically,

• Certificates of Analysis from a manufacturer of media/(b) (4) that are used in the production of the product (b) (4), CMRL 1066 (b) (4), and who also manufactures (b) (4) (HEPES and CMRL 1066 Transplant Solution), state that these solutions are not sterile [Sterility Assurance Level (SAL) of (b) (4)]. All such (b) (4) specifications have been approved by your firm's Quality Unit and (b) (4) were released for use in aseptic operations.

• Your firm uses the SOP, Material Management Program, QAL—SOP—402, to manage the acceptance of (b) (4) (b) (4), such as (b) (4). This SOP is linked to specifications that require sterility testing of (b) (4). Both the material management SOP and specifications are approved by your firm's Quality Unit. An (b) (4) sterility method is used as part of acceptance of (b) (4). The related sterility method validation only addressed (b) (4) media (b) (4) and one (b) (4). However, the validation is also used to support the sterility testing of other (b) (4) and media that are used in production or are part of the final product.

Establishment of the reliability of the (b) (4) suppliers' report of analysis is deficient in that the test results are not appropriately validated at appropriate intervals. Specifically:

• Your firm has not established the reliability of suppliers' Certificate of Analysis for, but not necessarily limited

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to, the following (b) (4) : (1) CMRL 1066 (Transplant Solution) and (2) HEPES, specification (b) (4) respectively. For CMRL 1066, tests include (b) (4) . For HEPES, tests include (b) (4) .

• Your firm has not established the reliability of suppliers' Certificate of Analysis for the following (b) (4) (b) (4) (Specification (b) (4) and (b) (4) (Specification (b) (4) For (b) (4) , tests include (b) (4)

Drug product (b) (4) testing is deficient in that at least one specific test to verify the identity of each (b) (4) is not performed. Specifically,

• Your firm does not conduct identity testing for, but not necessarily limited to, the following excipients that are included in the final product: (1) CMRL 1066 (Transplant Solution) and (2) HEPES, specification (b) (4) and (b) (4) , respectively.

Observation 10

Lack of assessment of (b) (4) Specifically,

• Your firm has not assessed for (b) (4) impurities regarding single (b) (4) parts (e.g., (b) (4)) and sterilized (b) (4) that are used in manufacturing of the product.

• Your firm has not assessed for (b) (4) impurities for your drug product containers: (b) (4) (Specification (b) (4) (Specification (b) (4) .

Observation 11

Your firm failed to establish a (b) (4) sample program and did not retain (b) (4) samples for drug products for

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(b) (4)

Observation 12

Carbon dioxide gas used in incubator is not routinely monitored for chemical quality, oil, or particulate levels and no COA is available to describe gas quality.

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