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	July 9-17, 2018* FEI NUMBER 3005241015

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Woo Sung Kee, Vice Chairman/CEO

FIRM NAME	STREET ADDRESS
Celltrion Inc.	23 Academy-Ro, Yeonsu-Gu
CITY, STATE AND ZIP CODE	**TYPE OF ESTABLISHMENT INSPECTED**
Incheon City, 406-840, Republic of Korea	Sterile Injectable Drug Product and 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 FIRM (I) (WE) OBSERVED:

OBSERVATION 1

There are no written procedures for production and process controls designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess.

Specifically,

Your firm failed to implement written procedures to adequately manage glass vial breakage that may occur during drug product filling operations after the vial washing step. For example, two vials were broken as documented on batch (b) (4) at 14:24 on April 5, 2018. The batch record states, "The debris and vials around the affected areas were removed in filling room (b) (4) ". The record does not state how many vials were removed or any additional details. Your firm has no written procedure to ensure the vials that have the potential to be compromised with glass particles are removed from the filling line.

In addition, the batch record for (b) (4) states on March 25, 2018, at (b) (4) "broken vials were found at the outlet of the (b) (4) zone" during the filling process. However, the filling operations continued until (b) (4) The outlet of the (b) (4) zone leads to the (b) (4) that feeds empty glass vials to the filling line. Your firm lacks adequate documentation to ensure vials that may have been compromised with glass particles did not proceed to the filling step.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (*Print or Type*)	DATE ISSUED
		Ashar P. Parikh, Investigator Richard Ledwidge, Biologist Jacek Cieslak, Chemist	07/17/2018

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OBSERVATION 2

Employees engaged in the processing of a drug product lack the training required to perform their assigned functions.

Specifically,

Your firm performs 100% visual inspection on finished (b) (4) drug product. Your qualification for the operators is inadequate in that the (b) (4) qualification vials with glass particles are on the (b) (4) of the (b) (4) (b) (4) not (b) (4) the (b) (4) at the (b) (4) of the vial. Your firm only utilizes photographs for training on this defect, however these photographs are unclear and inadequate to identify glass particles in vials. Without an adequate qualification vial, your firm cannot ensure your operators can observe this defect during 100% visual inspection.

Furthermore, the review of the visual inspection qualification records revealed your firm does not have a procedure to address an employee who repeatedly failed to identify a specific defects during all (b) (4) qualification runs as observed during the most recent qualification for Operator (b) (6) performed in January 2018.

OBSERVATION 3

Routine checking of automatic equipment is not performed according to a written procedure designed to assure proper performance.

Specifically,

Your firm utilizes a (b) (4) sensor to reject drug product vials that have not been (b) (4) (b) (4) prior to the capping process. However, your firm does not perform challenge testing of the sensor prior to running (b) (4) batch of drug product. In addition, your firm does not document the (b) (4) the sensor is set to in the batch record.

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OBSERVATION 4

Procedures describing the calibration of instruments, apparatus, gauges, and recording devices are deficiently written or followed.

Specifically,

Your firm does not adequately monitor the (b) (4) incubator rooms used to incubate environmental, media fill, and sterility samples. Your most recent temperature mapping study determined hot and cold spots for the incubators however your routine temperature monitoring gauge is not located in these areas.

OBSERVATION 5

Your firm confirmed the presence of (b) (4) on the surface of the (b) (4) culture fluid in the (b) (4) L bioreactor as stated in deviation report DE-P2-17-170. The (b) (4) were first documented in 2017, during post PPQ (b) (4) L bioreactor runs. Your firm has not identified the composition of these (b) (4).

OBSERVATION 6

On July 11, 2018, during the walkthrough of the (b) (4) unit operation, we observed the transfer of harvest tank (b) (4) to the (b) (4) load tank. The distance the harvest (b) (4) must travel from the harvest tank to the (b) (4) load tank is > (b) (4) and requires connecting (b) (4) transfer hoses between the (b) (4) (b) (4) All (b) (4) connections are performed in an open ISO 8 environment without environmental monitoring during unit operation. The (b) (4) connection requires more than (b) (4) of open exposure because (b) (4) of (b) (4) must be (b) (4) from the transfer line, prior to making the open hose connection to the (b) (4) (b) (4) In addition, your firm identified the open hose connections as the root cause for the out-of-specification bioburden result for (b) (4) load, lot# (b) (4), documented in Deviation DE-P2-17-167.

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OBSERVATION 7

On July 9, 2018, during the walkthrough of the (b) (4) unit operation in Suite (b) (4), we observed (b) (4) product, (b) (4) formulation (b) (4) and excipient (b) (4) on the floor and (b) (4) basin. While walking through the room, our shoe covers were (b) (4) to the floor which was attributed to the (b) (4) in the excipient (b) (4). Your firm had no procedures in place to address downstream spills. Lastly, there are no additional (b) (4) purifications steps as this is the final unit operation prior to transfer into a holding bag and drug substance filling.

OBSERVATION 8

During the review of QC equipment logsheets, we observed your firm failed to document the time and temperature of release, stability, and reference standard samples during transfer between freezers. For example:

- (b) (4) samples from freezer LEQ-94297 (b) (4) C) located in Suite C2 372, were transferred to LEQ-94201 for Maintenance of Validation (MOV) on June 6, 2018
- (b) (4) stability samples from freezer LEQ-94255 (b) (4) C) located in Suite W2 307, were transferred to FC103 for MOV execution on September 19, 2017
- (b) (4) samples from freezer LEQ-93097 (b) (4) C) located in Suite W2 302 transferred to LEQ-93098 on August 31, 2017

In addition, your firm had not established sampling handling procedures to ensure the frozen samples are not exposed to room temperature for extended periods of time during transport from one storage location to another.

*DATES OF INSPECTION
7/09/2018(Mon), 7/10/2018(Tue), 7/11/2018(Wed), 7/12/2018(Thu), 7/13/2018(Fri), 7/16/2018(Mon), 7/17/2018 (Tue)

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	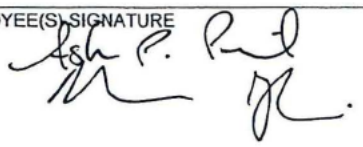	Ashar P. Parikh, Investigator Richard Ledwidge, Biologist Jacek Cieslak, Chemist	07/17/2018