DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

| DISTRICT ADDRESS AND PHONE NUMBER | DATE(S) OF INSPECTION |
|---|---|
| Food and Drug Administration - New Jersey District, 10 Waterview Blvd, 3rd Floor, Parsippany, NJ 07054 973-331-4900<br><br>Industry Information: www.fda.gov/oc/industry | 11/12/2019-11/26/2019*<br>FEI NUMBER<br>3002889358 |

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Nellie D. Clark Eliza, VP Site Head of Manufacturing

| FIRM NAME | STREET ADDRESS |
|---|---|
| ImClone Systems, L.L.C. | 33 ImClone Drive |
| CITY, STATE, ZIP CODE, COUNTRY | TYPE ESTABLISHMENT INSPECTED |
| Branchburg, NJ 08876-3904 | Biological 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 WE OBSERVED:

## OBSERVATION 1

Appropriate controls are not exercised over computers or related production systems.

Specifically, electronic data obtained from manufacturing process or related equipment are not appropriately controlled. For example,

A. We observed from the audit trails of the (b) (4) units that electronic files identified as Calibration Study, Qualification Study and Verification Study have been deleted. These (b) (4) (b) (4) units are used for the equipment qualifications, involving (b) (4) processes. The deleted incidents and related audit trail were not reviewed by the quality unit. For example, the following are some of the actions observed in the audit trail obtained from the (b) (4) (b) (4) units.

| (b) (4) Unit | Date/Time | Actions |
|---|---|---|
| | 31-Jan-2018 at 15:57:48 | Qualification Study : (b) (4) deleted by User ID (b) (6)". User Name: (b) (6) |
| | 01-Feb-2018 at 09:22:17 | Qualification Study : (b) (4) " deleted by User ID : (b) (6). User Name: (b) (4) |

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|---|---|---|
| | Tamil Arasu, Investigator Tamil Arasu<br>Guerlain Ulysse, Investigator Guerlain Ulysse | 11/26/2019 |

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| | | |
|---|---|---|
| (b) (4) | 05-Feb-2018 at 14:15:14 | Verification Study : (b) (4) " deleted by User ID : (b) (6)". User Name: (b) (6) |
| | 05-Feb-2018 at 14:17:03 | Calibration Study : (b) (4) " deleted by User ID : (b) (4)". User Name: (b) (4) |
| | 05-Feb-2018 at 14:17:19 | Calibration Study : "(b) (4) " deleted by User ID : (b) (4)". User Name: (b) (4) |
| | 05-Feb-2018 at 14:17:38 | Verification Study : " (b) (4) deleted by User ID : (b) (4). User Name (b) (4) |
| | 05-Feb-2018 at 14:18:05 | Verification Study : (b) (4) deleted by User ID : "(b) (4). User (b) (4) |
| | 05-Feb-2018 at 14:20:22 | Qualification Study : "(b) (4) " deleted by User ID : (b) (6)". User Name: (b) (6) |
| | 22-Feb-2018 at 07:06:39 | Qualification Study : (b) (4) deleted by User ID : (b) (6). User Name: (b) (6) |
| | 23-Mar-2018 at 09:01:04 | Qualification Study : (b) (4) deleted by User ID : (b) (6) User Name: (b) (6) |
| | 13-Apr-2018 at 09:57:49 | Qualification Study : "(b) (4) deleted by User ID : (b) (6)". User Name: (b) (6) |

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|---|---|---|
| | Tamil Arasu, Investigator (TA)<br>Guerlain Ulysse, Investigator Guerlain Ulysse C.U. | 11/26/2019 |

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| | | |
|---|---|---|
| | 16-Aug-2018 at 13:49:53 | Qualification Study : (b) (4) deleted by User ID : (b) (6). User Name: (b) (6) |
| | | |
| | 05-Feb-2018 at 14:15:14 | Verification Study: (b) (4) deleted by User ID: (b) (6)". User Name (b) (6) |
| | 05-Feb-2018 at 14:17:03 | Calibration Study: (b) (6) deleted by User ID: (b) (6). User Name (b) (6) |
| | 05-Feb-2018 at 14:17:19 | Calibration Study: (b) (4) deleted by User ID: (b) (6)". User Name: (b) (6) |
| (b) (4) | 05-Feb-2018 at 14:17:38 | Verification Study: (b) (4) deleted by User ID: (b) (6) User Name: (b) (6) |
| | 05-Feb-2018 at 14:18:05 | Verification Study: (b) (4) " deleted by User ID: (b) (6). User Name: (b) (6) |
| | 05-Feb-2018 at 14:19:51 | Qualification Study: (b) (4) deleted by User ID: (b) (6) User Name: (b) (6) |
| | 13-Apr-2018 at 09:57:49 | Qualification Study: "(b) (4) deleted by User ID: (b) (6). User Name: (b) (6) |

** Full name withheld, and only initials shown*

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B. Review of the (b) (4) unit's (Serial No (b) (4)) audit trail also indicated users had logged into the system on multiple occasions to do Audit Trail operations followed by adjusting the system clock. For example, the following table shows three sequential actions recorded in the audit trail:

| (b) (4) | Date/Time | Actions |
|---|---|---|
| (b) (4) | 28-Sep-2018 at 10:50:13 | User Id : (b) (6) Logged in to System. |
| | 28-Sep-2018 at 11:03:47 | User Id : (b) (6) . User Name: (b)(6) * logged in to do "AuditTrail" operation in (b) (4) screen |
| | 28-Sep-2018 at 10:48:59 | (b) (4) Clock adjusted from 28/09/2018 11:03:47 to 28/09/2018 10:49:00 by User Id : (b) (6). User Name: (b) (6) |

** Full name withheld, and only initials shown*

Similar actions were observed in (b) (4) units, (b) (4) and (b) (4) as well. The firm's quality unit did not review the audit trails from these (b) (4) units. Operators were assigned administrative privileges. In addition, the firm does not have sufficient controls to prevent the deletion of electronic data stored in these systems, which is not backed-up on a periodic basis.

C. We observed that test runs have been aborted from (b) (4) Test Instruments and the aborted tests were not logged in the user logs, documented or reviewed. For example, review of the run history on the (b) (4) Test Instruments (ID: (b) (4)) indicated an error message "Test aborted by the operator" on multiple occasions. However, these events were not

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documented in the user logs and reviewed by the quality unit. We were unable to ascertain why the operators had aborted the runs. These (b) (4) Test Instruments are used to conduct (b) (4) and (b) (4) testing of (b) (4) that are used in the manufacturing processes of biological drug substances such as Cetuximab, Ramucirumab, Necitumumab and Galcanezumab, which are utilized in the production of drug products that are distributed in the U.S. market.

**OBSERVATION 2**

Appropriate controls are not exercised over computers or related laboratory systems.

Specifically, Quality Control (QC) laboratory data stored on multiple stand-alone equipment computer systems are not secured from modification or deletion. We observed that QC laboratory personnel could delete an entire folder found within the firm's shared drive "(b) (4) where data derived from stand-alone QC laboratory equipment computer systems are stored. For example, a QC laboratory employee demonstrated that they could create a test data folder and delete that folder from the computer system attached to the UV spectrometer (Software: (b) (4) Other computer systems where data is not secured include, Plate Reader (Software: (b) (4) ), UV-Vis (Software: (b) (4) ), qPCR (Software (b) (4) qPCR (Software: (b) (4) ), (b) (4) Densitometer (Software: (b) (4) ) and FTIR (Software: (b) (4) ). These laboratory instruments are routinely used for testing of drug substances such as Cetuximab, Ramucirumab, Necitumumab and Galcanezumab, which are utilized in the production of drug products that are distributed in the U.S. market.

***DATES OF INSPECTION**

11/12/2019(Tue), 11/13/2019(Wed), 11/14/2019(Thu), 11/15/2019(Fri), 11/18/2019(Mon), 11/19/2019(Tue), 11/20/2019(Wed), 11/21/2019(Thu), 11/25/2019(Mon) and 11/26/2019(Tue)

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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 judgment, 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."