DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
CDER Division of Inspectional Assessment; Attn. Mahesh Ramanadham, Director E-MAIL: Mahesh.Ramanadham@fda.hhs.gov; PHONE +1-301-796-3272 Mail address: 10903 New Hampshire Ave. White Oak Building 51, Room 4328 Silver Spring, MD-20993 Industry Information: www.fda.gov/oc/industry	August 6 to August 14, 2018
	FEI NUMBER 1000526871

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Michael Pehl, Chief Executive Officer

FIRM NAME	STREET ADDRESS
Immunomedics, Inc.	300 The American Road
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Morris Plains, NJ-07950	Drug Substance Intermediate Manufacturing Facility

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

1. The quality control unit lacks authority to investigate critical deviations of approved procedures. Specifically, the discovery of a data integrity breach in February 2018 did not trigger a deviation. The scope of the data integrity breach included manipulation of bioburden samples, misrepresentation of the (b) (4) integrity test procedure in the batch record and backdating of batch records, including dates of analytical results.

2. There is no assurance that samples and batch records from the (b) (4) process validation and commercial batches manufactured prior to February 2018 were not impacted by the data integrity breach. Interviews by Immunomedics to personnel involved in the event were conducted under attorney/client privilege and no additional documentation is available, therefore no assessment could be made during the prelicense inspection in support of (b) (4)

3. Retesting procedure for the (b) (4) is inadequate. Specifically:
   a. SOP-0162 "Out of Specification Investigations" indicates that "if the company believes there is possibility the laboratory test did have error, and the error was undetected, then the company may wish to perform a retest." OOS Investigation report 18-001 shows that routine retesting was performed due to an initial OOS result.
   b. SOP-0162 allows for retesting of microbiology samples. An OOS result for the (b) (4) n-process bioburden sample was recorded on (b) (4). A retest was conducted using a retain sample on 1/5/2018 and the results on 1/10/2018 were OOS (OOS 18-001). Initiation of a non-conformance report (NCR 18-009U) was delayed until the results of the retest were reported on 1/10/2018.

4. The raw material sampling and testing program is inadequate. Specifically:
   a. (b) (4) supplied by (b) (4) has never been sampled and there is no assurance that the manufacturer can consistently provide material meeting specifications. The solution is (b) (4) from the vendor and is (b) (4) cell culture bioreactors. Deviations 18-081U and 18-163U were initiated due to contamination in the production bioreactors. In

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both cases, probable root causes included the (b) (4) addition assembly (b) (4) bag, line, and valve). Testing of an unused (b) (4) bag in inventory also resulted in a positive sample.

b. Product-contact (b) (4) and (b) (4) used during cell culture of the (b) (4) are not tested for bioburden.

5. The firm lacks procedures for inventory audit trail and for tracking and reconciliation of raw materials used to manufacture the (b) (4) Specifically:
   a. The firm does not keep records tracing the use of raw material. Raw material reconciliation cannot be conducted as discarded raw materials are not documented. During the tour to the manufacturing facility on 8/6/2018, the inspection team observed a (b) (4) L container of (b) (4) (b) (4) in the loading dock for destruction. The material could not be traced.
   b. Warehouse raw material inventory list is kept in an Excel Spreadsheet that lacks history traceability. During the tour of the warehouse on 8/6/2018 Warehouse inventory cannot be located using the Excel Spreadsheet. Specifically, (b) (4) (catalog # (b) (4) Lot # (b) (4) (b) (4) was present in the warehouse, however the location and inventory could not be provided.
   c. The warehouse is not adequately mapped for inventory purposes with floor plans. Items stored on the floor have no assigned location. In addition, quarantine and released items on the floor are kept side-by-side without a system in place to prevent the use of quarantined raw material.

6. Differential pressure between GMP areas of different area classification is not adequately maintained and monitored. Specifically,
   a. Air pressure in the GMP areas is not adequately maintained. For example, differential pressure between Rooms (b) (4) (Class C (b) (4) and (b) (4) (Class D corridor) was out of action levels in 37 out of (b) (4) measurements between July 24, 2018 and August 1, 2018.
   b. Continuous monitoring of pressure in the GMP areas has been installed in July 2018 and is undergoing qualification, however not all adjacent rooms with different air classification are alarmed for low pressure differential. For example, differential pressure between the Rooms (b) (4) (Class C (b) (4) (b) (4) and (b) (4) (Class D corridor) is not alarmed.

7. The design of the facility is inadequate in that no drains are present in the (b) (4) rooms. In addition, there is no SOP for liquid containment and disposal after a catastrophic spill. All process (b) (4)

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the Production Bioreactor are held in (b) (4) bags.

8. There is no signed Quality Agreement between (b) (4) and Immunomedics Inc. (b) (4) is the supplier of cell culture media and all buffers, solutions (including (b) (4), and chromatography resins used for (b) (4) of the (b) (4)

9. No procedure is in place for (b) (4) trending of results. During the process validation (b) (4) campaign, bioburden levels in the chromatography resins were not trended and inadequately high bioburden levels were not investigated. Low level bioburden ((b) (4) CFU/ (b) (4) mL) was observed in the (b) (4) resin chromatography after sanitization in (b) (4) batches (b) (4) and the bioburden level increased to too numerous to count in (b) (4) batch (b) (4) No deviation was initiated.

10. Deviation investigations and CAPA implementations are inadequate. For example, Deviation 18-053U was initiated after an internal audit concluded that the (b) (4) had not been adequately tested for integrity (b) (4) (b) (4) The deviation included the following deficiencies:
    a. Lot number in the deviation form indicates "multiple lots" without specifying the potential lots impacted.
    b. Product impact assessment includes the conclusion of a clinical Health Hazard Assessment, but no risk assessment on the presence of (b) (4) in the product is documented.
    c. The CAPA section indicates that remediation included "… purchasing additional test equipment to evaluate the (b) (4) ts use." However, at the date of the inspection no additional equipment has been purchased and no information about the CAPA is documented in the deviation.

11. Deviation initiation and closing times are inadequate. Specifically:
    a. SOP-0152 "Deviation handling" indicates that if the deviation cannot be completed by the assigned due date, a one-time extension can be requested to the QA unit. The following deviations were not closed by the due date and did not include an extension:
        i. 18-116U: deviation due date was 7/20/2018; deviation was open at the time of the inspection
        ii. 18-081U: deviation due date was 6/17/2018; deviation was open at the time of the inspection
        iii. 18-079U: deviation due date was 6/16/2018; deviation was closed on 8/3/2018
        iv. 18-050U: deviation due date was 5/9/2018; deviation was open at the time of the inspection

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	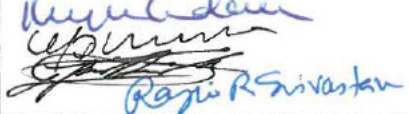	Reyes Candau-Chacon, Microbiologist; Madushini Dharmasena, Staff Fellow; Gunther Boekhoudt, Staff Fellow; Rajiv Srivastava, CSO	08/14/2018

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b. SOP-0152 "Deviation Handling" does not specify a time limit between time/discovery of event and deviation initiation. The following deviations were initiated more than one month after event discovery:
   i. 18-009U: investigation into bioburden OOS #18-001 for (b) (4); date of event was 1/10/2018, deviation was initiated on 3/27/2017.
   ii. 18-053U: (b) (4) related discrepancy; date of event was February 2018, deviation was initiated on 4/9/2017

12. Cleaning of (b) (4) equipment, including (b) (4) and product-contact parts of the (b) (4) is not validated or verified. Non-conformance report 18-009 initiated due to a (b) (4) OOS bioburden sample includes as the primary root cause the (b) (4) contaminated during vendor pressure testing.

13. The procedure to prevent contamination of the (b) (4) after (b) (4) is inadequate for a product stored 2 to 8°C for up to (b) (4) Specifically, during a mock (b) (4) and dispensing of an (b) (4) surrogate conducted on August 9, 2018, the following was observed:
   a. After (b) (4) the surrogate was transferred first to a (b) (4) L bag (b) (4) B) and then from the (b) (4) B to (b) (4). The (b) (4) B was removed from its container and assembled in the Biologic Safety Cabinet (BSC) used for (b) (4) and dispensing. Multiple (b) (4) process manipulations were conducted to prepare the (b) (4) B, including cutting, closing, and connecting several lines and assembly of the (b) (4) to the (b) (4) B.
   b. During the (b) (4) B preparation process, the end of the tubing (b) (4) was observed to touch the operator's hands, the surfaces of the BSC, and the material placed inside the BSC.
   c. Prior to filling the (b) (4) analytical samples were collected into (b) (4) ml (b) (4) tubes. The diameter of the tubing (b) (4) inch; (b) (4) mm) used to fill the tubes and the (b) (4) tubes (b) (4) mm) are similar. In addition, the flow of the (b) (4) surrogate was not continuous and was difficult to control. As a result, the surrogate was spilled during the sampling process.

RC, 8/14/2018

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