DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
US FDA/CBER Office of Compliance and Biologics Quality 10903 New Hampshire Avenue W071-5128 Silver Spring, MD 20993-0002 TEL: (240) 402-9159/ FAX (301) 595-1304 Industry Information: www.fda.gov/oc/industry	March 12 -16, 2018 FEI NUMBER 3003208230

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Peter Patrick Janssen, Chief Executive Officer

FIRM NAME	STREET ADDRESS
Plasma Industries Belgium SCRL	Avenue De Tyras 109
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
B-1120 Brussels, Belgium	Biologics 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

The CIP cleaning validation of Vessel (b) (4) documented under Document (b) (4) entitled "CIP for (b) (4) vessel (b) (4) on (b) (4) did not include a justification for not (b) (4) an area of the vessel (vessel (b) (4) that is known to not be (b) (4) by the (b) (4) This vessel is used to contain non-US plasma (not used for (b) (4) as well as (b) (4) The (b) (4) is used to (b) (4) to and (b) (4) the (b) (4) ot, centrifuges and for the swelling of the (b) (4) used in the (b) (4) manufacturing process.

Observation #2

The following deviations (Events) related to (b) (4) were not initiated in a timely manner or are otherwise inadequate:

A. Deviation Investigation 79659 initiated 18 August 2016 was opened due to unknown substance (later identified as plasma) found in the (b) (4) and (b) (4) of centrifuges (b) (4) during a shutdown. The investigation is inadequate in the following:

i. Lots of the drug substance manufactured prior to the shutdown was not evaluated as part of product impact.

ii. The preventative maintenance of the centrifuges, including the centrifuge (b) (4) was not evaluated.

iii. The last batch manufactured before the shutdown and the discovery of plasma in the (b) (4) (b) (4) of the centrifuge was not tested to show there was no impact downstream of the centrifugation step; the investigation was closed concluding no impact on product.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE *(Print or Type)*	DATE ISSUED
	Susan Jackson	**Susan Jackson, CSO** **Mihaly Ligmond, CSO**	**March 16, 2018**

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iv. The investigation failed to address if the process is validated.

v. Investigation failed to address the root cause for plasma overflow into the (b) (4) (b) (4).

B. Event 104972 which was opened due to the detection of particles during the changing of (b) (4) (b) (4) was opened on 22-Nov-2017 however the date detected was 22-Sep-2017. This deviation was still open during the current inspection.

C. Event 105703 which was opened due to the detection of particles on (b) (4) was opened on 05-Dec-2017 however the date detected was 16-Nov-2017.

D. Event 105710 which was opened due to the detection of particles on a (b) (4) of (b) (4) was opened on 05-Dec-2017 however the date detected was 16-Nov-2017.

E. Event 107670 which was opened due to the detection of particles during the changing of (b) (4) (b) (4) was opened on 11-Jan-2018 however the date detected was 15-Dec-2017.

F. Event 109750 which was opened due to the detection of particles on (b) (4) of (b) (4) was opened on 13-Feb-2018 however the date detected was 11-Jan-2018.

G. Event 74734 was opened due to the detection of particles while changing (b) (4). The particles found included particles identified as most likely derived from (b) (4). The quality impact assessment states that the particles found are (b) (4) however it does not state that (b) (4) (b) (4) are not normal (b) (4) and no specific assessment regarding the presence of these (b) (4) is documented.

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H. Event 94220 which was opened due to the detection of particles during the changing of (b) (4) has 2 overdue CAPAs. CAPA 103334 was due 31-Dec-2017 and CAPA 103335 was due 31-Jan-2018. The due dates for these CAPAs have not been extended by the Quality Unit.

Observation #3

The current procedure for CIP of the (b) (4) fails to require the initiation of a deviation when an atypical event is detected during the (b) (4) of the (b) (4) Specifically, CAPA 81235 was initiated as part of Event Record 79659 to update SOP (b) (4) (b) (4) 1879 version 3.0 to include a (b) (4) clean and (b) (4) (b) (4) clean. This procedure does not require the operator who performs the (b) (4) clean or a (b) (4) clean to initiate a deviation when a (b) (4) substance is observed in the (b) (4) (b) (4) of the centrifuge used during the (b) (4) process.

Observation #4

The change to the use of a new (b) (4) for the (b) (4) of the (b) (4) was implemented on February 27, 2018 however the associated change control (Change Control 92345) remained open as of March 15, 2018. As per Document (b) (4) 0527 entitled "Change Control" "(b) (4) (b) (4) (b) (4) ..." This form was not completed for this change control.

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Observation #5

As per Document (b) (4) 2716 entitled "Particle Contamination" a deviation (Event) is not required to be initiated for the detection of particles until particle identification is (b) (4) which is allowed to (b) (4).

Observation #6

There is no written justification for the clarifying (b) (4) limits of (b) (4) as stated in Document (b) (4) 2262 / 14.0 entitled (b) (4) 2261 – Appendix 1: Production File (b) (4) ' which is a portion of the (b) (4) batch record.

Observation #7

The preventative maintenance program for the (b) (4) which is used to prepare (b) (4) for the (b) (4) process and the (b) (4) used for CIP was not adequately conducted in year 2016 and 2017. The preventative maintenance program did not require a (b) (4) of the (b) (4) (i.e. (b) (4) (b) (4)) at a defined frequency. Specifically,

A. The executed preventative maintenance records for the year 2016 and 2017 for the (b) (4) (b) (4) and the (b) (4) does not account for all components and the frequency of maintenance on each component.

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B. No corrective and preventative measures were implemented for (b) (4) detected in the (b) (4) (b) (4) detected in 2017.

C. On March 12, 2018, during a walk-through of the facility, (b) (4) discoloration was observed (b) (4) (b) (4). The firm explained that the discoloration is due to (b) (4) and that this level of (b) (4) has no product impact.

Observation #8

Discoloration resembling (b) (4) was observed on (b) (4) located in the (b) (4) of the Operations Building Room (b) (4) during a walkthrough of the area on 3-12-18. Open operations related the manufacturing of (b) (4) such as the addition of (b) (4) components into (b) (4) used in the (b) (4) and (b) (4) process are performed in this room.

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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."