DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10903 New Hampshire Ave., Bldg. 51, Room 4225 Silver Springs, MD 20993 (301) 796-3334 FAX: (301) 847-8738 Industry Information: www.fda.gov/oc/industry	12/8-16/2016
	FEI NUMBER 3007255826

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Aldo Braca, CEO & President

FIRM NAME	STREET ADDRESS
BSP Pharmaceuticals S.p.A.	Via Appia km 65.561
CITY, STATE AND ZIP CODE Latina, Italy 04013	TYPE OF ESTABLISHMENT INSPECTED Drug 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 [redacted] (WE) OBSERVED:

1. All automatic mechanical, or electronic equipment, used in the manufacture, processing, packing, and holding of your drug product is not checked according to a written program designed to assure proper performance. Specifically, your master validation plan does not specify duties and responsibilities for validation activities conducted on contractual basis by outside service providers.

2. Input to and output from computer related systems was not adequately checked for accuracy. Specifically,
a) (b) (4) and (b) (4) system's alarm messages appearing on associated computer display screens following acceptance test set up an execution were not being documented as they actually appeared on the display screen for comparison to the validation acceptance tests expected results.
b) After the quality unit added new LIMS functions for QC analysts to enter data into LIMS, without testing and training, the new function was made available to the analysts and was failed for the first time use:

(1) On October 30th, 2015, for the first time to enter the results of bacterial endotoxin test for (b) (4) sterile into LIMS, "< (b) (4) ", a conformed data, was entered into LIMS but LIMS returned it as "non conformance".

(2) On November 21st, 2016, for the first time to enter the results of bacterial endotoxin test (BET) for a stopper into LIMS, "< (b) (4) EU/Stopper", a conformed data, was entered into LIMS but LIMS returned it as "non conformance."

3. Batch control records do not include complete information relating to the control of each batch. Specifically, the light intensity readings from your luxmeters measuring light intensity at your visual inspection tables were being documented in the batch records without being corrected for the deviations from the standards to which they were calibrated.

[redacted]
Add Continuation Page

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (*Print or Type*)	DATE ISSUED
	Francis Guidry [signature]	Francis Guidry /Investigator Xiaokuang Lai / Microbiologist	12/16/2016

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4. Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not followed. Specifically, On March 9th, 2016, during filling process for manufacturing [redacted] mg batch [redacted] in Sterile [redacted] the difference of air pressure between the filling exit for personnel, a Grade B area, and the [redacted] room, a Grade C area, was lost to 0 for 18 minutes. This pressure difference was maintained at [redacted] Pascal during normal manufacturing. After the pressure difference was restored, no additional monitoring for the environment in the filling room was conducted; and no additional microbiological tests were conducted for the finished product. The product was released on June 10th, 2016 and shipped to the US on June 28th, 2016.

5. Employees engaged in the manufacture of a drug product lack the training required to perform their assigned functions. Specifically, on October 20th, 2016, an environmental surface sample yielded [redacted] cfu/25 cm^2 in a Grade C area, which was out of the action limit of > [redacted] cfu/25 cm^2 for a Grade C area. After investigation, the root cause was determined as a human error, not properly following the gowning procedure. However, no re-training or any other actions were taken to prevent the reoccurrence of this kind of error.

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NOTE: Observation 4 removed following a discussion of the conditions surrounding the incident describes in the original FDA-483.

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