DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
FDA / CBER / Office of Compliance and Biologics Quality 10903 New Hampshire Avenue WO71 - 5128 Silver Spring, MD 20993-0002 TEL: (240) 402-9159	June 3-June 24, 2019
	FEI NUMBER 3002875226

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Russell E. Thirsk, Head of Belgium Operations

FIRM NAME	STREET ADDRESS
GlaxoSmithKline Biologicals SA	89 rue de l'Institute
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
1330 Rixensart Belgium	Vaccine 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:

1. Laboratory controls do not include the establishment of scientifically sound and appropriate specifications designed to assure that in-process materials conform to appropriate standards of purity. Specifically,
   a. (b)(4), for the following steps in (b)(4), the acceptance criteria or specification for the Microbial Purity test on (b)(4) is (b)(4) (b)(4) (b)(4).

   b. There is insufficient bioburden and endotoxin monitoring throughout the manufacturing processes for the following bulk products: (b)(4), Shringrix, and (b)(4) (b)(4). For example, during routine production, Shingrix is tested for bioburden from the (b)(4) and bioburden and endotoxin samples are taken (b)(4) sterile filtration.

2. Failure to thoroughly investigate the presence of (b)(4) in the Water for Injection (WFI) (b)(4) where sterile bulk (b)(4) is manufactured. The deviation investigations failed to evaluate complaints for (b)(4) received (if any) since the (b)(4) (b)(4) on the WFI (b)(4) on December 4, 2015, the attributing root cause.
   a. Deviation 200578478 was initiated on 28 July 2017 in Building (b)(4) at the (b)(4) of the WFI --. The (b)(4) were identified as (b)(4).
   b. Deviation 200654818 initiated on 26 July 2018 in Building (b)(4) in WFI (b)(4). The root cause also attributed to the 04 December 2015 (b)(4).

3. The following corrective actions were found deficient:
   a. The corrective actions/preventative actions to multiple deviations opened in 2016 which stopped production until November 2016 is deficient in that there was no assessment of the current automated (b)(4) for equipment to ensure that the cycle was adequate for the (b)(4) contamination. This equipment includes (b)(4)),

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) NAME AND TITLE *(Print or Type)*	DATE ISSUED
	Debra M. Emerson, Investigator **Susan Jackson, Investigator** **Leslie Wagner, Chemist** **Shuang Tang, Biologist**	**6/24/19**

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(b)(4) used in the production of (b)(4) bulk.

b. As a correction to Observation 1a from the January 9-27, 2017 inspection, the cleaning validations performed are incomplete as there were no surface swabs taken from any hard to clean area(s), and the equipment and associated (b)(4) was not opened after each cleaning run to ensure that the equipment was visibly clean. This applies to (b)(4) used to manufacture (b)(4) bulk.

c. The corrective action to 1c from the January 9-27, 2017 inspection, included a bactericidal efficacy study to justify not cleaning your dedicated (b)(4) and associated (b)(4) however this study failed to include known microbial isolates within the manufacturing areas such as (b)(4) and (b)(4).

4. Your firm has not performed adequate process validation for (b)(4) used in (b)(4) which have ranges in (b)(4) to include assessing each end of the range. For example,

(b)(4)

5. There is a lack of documentation approved by the Quality Unit to support operating outside of your routine operations. Specifically,

a. Deviation 200543472 was opened on 12 FEB 2017 when (b)(4) was found in the (b)(4) after (b)(4). The deviation determined that changes needed to be made to

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the automated system to ensure that the (b)(4) did not occur at the same time as the transfer of product into the [redacted].

b. As there were no work instructions for the operator, deviation 200558307 was opened on 02 MAY 2017 for [redacted] in the [redacted] after cleaning of the [redacted]. The [redacted] was changed on 05 May 2017.

6. The following equipment maintenance issues were on observed on June 7, 2019 in the [redacted] manufacturing building:

a. [redacted] material and a build-up of [redacted] was observed below a leaking [redacted] room.

b. A [redacted] was observed for the [redacted] in room [redacted] and in the [redacted] room.

c. [redacted] was observed above the [redacted] in various [redacted] to include the [redacted] and the [redacted].

d. A piece of a [redacted] was observed above the [redacted] in room [redacted].

e. [redacted] was observed dripping from a [redacted] for the [redacted] for [redacted] in the [redacted] room. The [redacted] from this [redacted] was also observed on the [redacted].

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."