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, Rm. 4235 Silver Springs, MD 20993 (301) 796-3334 Industry Information: www.fda.gov/oc/industry	06/04-08/2018; 06/11-14/2018
	FEI NUMBER 3002806419

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Frank Generotzky, Plant Manager

FIRM NAME	STREET ADDRESS
Baxter Oncology GmbH	Kantstr. 2
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Halle (Westf.), North Rhine-Westphalia, 33790	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 (I) (WE) OBSERVED:

PRODUCTION SYSTEM

OBSERVATION 1

Control procedures are not established which validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug product.

Specifically,
Your process validation of (b) (4) is deficient and your firm has not provided adequate assurance that the commercial manufacturing process is working as planned. One of (b) (4) process validation lots failed to meet release specifications prior to FDA approval. Since FDA approval, three of (b) (4) commercial lots have failed to meet release specifications.

A. Processes and functions identified in a risk analysis performed prior to process validation are not captured in the Process Validation Protocol (PPVA VV 34818e).

B. Control of manufacturing equipment variability was not included in the Process Validation Protocol (PPVA VV 34818e) or the Process Validation Report (PPVA VB 36315e, dated June 5, 2018). For example, neither report includes an evaluation of equipment such as tubing or vessels that are reused for different iterations of (b) (4) passes, nor do these reports evaluate using both (b) (4) and (b) (4) vessels as sources of (b) (4) (b) (4) for different iterations of (b) (4) passes.

Lot (b) (4), Lot (b) (4) and Lot (b) (4) have been released for commercial distribution to the U.S. market using this manufacturing process.

EQUIPMENT SYSTEM

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Emilie Kahn Luis M Burgos	Emilie E. Kahn, Investigator Luis M. Burgos Chemist	06/14/2018

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, Rm. 4235 Silver Springs, MD 20993 (301) 796-3334 Industry Information: www.fda.gov/oc/industry	06/04-08/2018; 06/11-14/2018
	FEI NUMBER 3002806419

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Frank Gencrotzky, Plant Manager

FIRM NAME	STREET ADDRESS
Baxter Oncology GmbH	Kantstr. 2
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Halle (Westf.), North Rhine-Westphalia, 33790	Manufacturer

OBSERVATION 2

Equipment used in the manufacture, processing, packing, or holding of drug product is not of appropriate design to facilitate operations for its intended use.

Specifically,

The (b) (4) System was not qualified for its intended use. For example, the system (b) (4) maintenance test used to qualify this equipment does not evaluate (b) (4) passing from (b) (4) vessels.

This equipment was used to manufacture Lot (b) (4) Lot (b) (4) and Lot (b) (4) which have been released for commercial distribution to the U.S. market.

QUALITY SYSTEM

OBSERVATION 3

The batch production and control records are deficient in that they do not include documentation of the accomplishment of each significant step in manufacturing.

The Batch Record (b) (4) HA 37570e/04 for Lot (b) (4) states that "If the (b) (4) achieves (b) (4) the (b) (4) will automatically (b) (4) to maintain (b) (4) near (b) (4) . From the point where the (b) (4) reaches (b) (4) continue (b) (4) for (b) (4) , then (b) (4) to (b) (4) before continuing with (b) (4) " Step (b) (4) requires the operator to record the time at "(b) (4) Achieved" and time at "(b) (4) during (b) (4) through the (b) (4) If (b) (4) is used for the (b) (4) pass, however, the batch record does not require the operator to note the time that (b) (4) was achieved and the time that the (b) (4) was (b) (4) for the subsequent (b) (4)

Lot (b) (4) used a (b) (4) for the same (b) (4) pass, and the peak (b) (4) was recorded at (b) (4) (b) (4) The batch record data cannot confirm whether the (b) (4) did not meet or exceed (b) (4) for more than (b) (4)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Emilie Kahn Luis M. Burgos	Emilie E. Kahn, Investigator Luis M. Burgos Chemist	06/14/2018

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10903 New Hampshire Ave. Bldg. 51, Rm. 4235 Silver Springs, MD 20993 (301) 796-3334 Industry Information: www.fda.gov/oc/industry	06/04-08/2018; 06/11-14/2018
	FEI NUMBER 3002806419

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Frank Generotzky, Plant Manager

FIRM NAME	STREET ADDRESS
Baxter Oncology GmbH	Kantstr. 2
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Halle (Westf.), North Rhine-Westphalia, 33790	Manufacturer

(b) (4) for the (b) (4). Lot (b) (4) was released for distribution in the U.S. market on May 31, 2018.

OBSERVATION 4

The responsibilities and procedures applicable to the quality control unit are not fully followed.

Specifically,
Document QK SV 26219e, Stability Monitoring Program for (b) (4) states that minimally (b) (4) batch per year out of the routine manufacturing" will be placed on stability. Your firm did not place a lot of (b) (4) on stability in 2015. Instead, a sample from Lot (b) (4) manufactured on August 8, 2015 was collected from finished product storage and placed on stability on October 28, 2016. A Non-Conformance Report was not created to document this departure from the quality-approved document.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Emilie Kahn Luis M. Burgos	Emilie E. Kahn, Investigator Luis M. Burgos Chemist	06/14/2018