

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT OFFICE ADDRESS AND PHONE NUMBER

10903 New Hampshire Avenue, Bldg. 71, Rm 5054
Silver Spring, MD 20993-0002
(240) 402-9160
orabioinspectionalcorrespondence@fda.hhs.gov
Industry Information: www.fda.gov/oc/industry

DATE(S) OF INSPECTION

09/18 - 09/29/2023*

FEI NUMBER

3002972083

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Alain Denis, Site Head

FIRM NAME

Sanofi Pasteur

STREET ADDRESS

1541 Avenue Marcel Merieux

CITY, STATE AND ZIP CODE

Marcy-L'Etoile, Metropole de Lyon, 69280

TYPE OF ESTABLISHMENT INSPECTED

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 (I) (WE) OBSERVED:

OBSERVATION 1

The master production and control records are deficient in that they do not include complete instructions. Specifically, there are no defined (b) (4) time frames and/or instructions for the (b) (4) preparation of the Concentrated Tetanus Protein (CTP) bulk in the Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate) manufacturing process.

A. The CTP bulk requires the (b) (4) of the bulk after the (b) (4) step in Bldg. (b) (4) (Room (b) (4)). The (b) (4) system is rinsed with a (b) (4) solution and collected into (b) (4) individual (b) (4) (b) (4) that are (b) (4) into a (b) (4) container, (b) (4) the CTP (b) (4) process. The CTP bulk is (b) (4) by the technician (b) (4) the (b) (4) container in a (b) (4) (b) (4) for an unknown specified amount of time under the biosafety cabinet. A bioburden sample is taken at this step at this step, (b) (4) the CTP bulk (b) (4) process.

B. The production batch record does not include instructions for the (b) (4) steps for the CTP bulk, (b) (4).

C. There is no validated mixing time-frame established for the CTP bulk concentration (b) (4) step to ensure (b) (4).

OBSERVATION 2

Written records of investigations into unexplained discrepancies and the failure of a batch or any of its components to meet specifications do not always include the conclusions and follow-up. Specifically,

A. Deviation record MLED22E3775 dated August 1, 2022, documents that two vials of (b) (4) (US Market

SEE
REVERSE
OF THIS
PAGE

/S/

EMPLOYEE(S) NAME AND TITLE (Print or Type)

Bumell M. Henry, Investigator
Travis S. Bradley, Investigator

DATE ISSUED

09/29/2023

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT OFFICE ADDRESS AND PHONE NUMBER 10903 New Hampshire Avenue, Bldg. 71, Rm 5054 Silver Spring, MD 20993-0002 (240) 402-9160 orabioinspectionalcorrespondence@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	DATE(S) OF INSPECTION 09/18 - 09/29/2023*
	FEI NUMBER 3002972083

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Alain Denis, Site Head

FIRM NAME Sanofi Pasteur	STREET ADDRESS 1541 Avenue Marcel Merieux
CITY, STATE AND ZIP CODE Marcy-L'Etoile, Metropole de Lyon, 69280	TYPE OF ESTABLISHMENT INSPECTED Vaccine Manufacturer

batch (b) (4) were observed to contain cellulose particles during visual inspection of retain samples related to a complaint of vial breakage (complaint no. 200255622). This lot had been released and distributed within the US market and was reported to the agency as a Biological Product Deviation Report (BPDR) on 09/15/2022. While reviewing the firm's CAPA investigation report MLED22A2877 pertaining to deviation MLED22E3775, it was observed that no effectiveness check was conducted to verify the effectiveness of the corrective action (updating instruction MLE-I-006038—clarifying the practice of the cutting of bags within filling line 14) implemented in response to the deviation.

B. While reviewing (b) (4) batch number (b) (4) (b) (4) for line (b) (4) utilized at the time for sterile (b) (4) of Act-Hib (US Market), it was observed that the (b) (4) batch was invalidated due to a reconciliation difference between the quantity of crimped vials (11,997) and the quantity of inspected vials (11,996) prior to being sent for (b) (4). Further review into the investigation of the discrepancy (Deviation MLED21E6490) revealed that the discrepancy was likely the result of a lost vial after the crimping step during transfer to visual inspection (b) (4). Due to the vial being lost, it could not be incubated and read for turbidity resulting in a potential impact to product manufactured on line (b) (4). While reviewing the firm's corrective actions pertaining to the deviation, it was observed that no corrective actions were implemented to prevent a recurrence of this event.

OBSERVATION 3

Drug products are not stored under appropriate conditions so that their identity, strength, quality, and purity are not affected. Specifically,

While observing warehousing operations within temperature controlled (2-8C) finished product storage room (b) (4) within the packaging warehouse, it was observed that one shrink wrapped pallet consisting of (b) (4) boxes (b) (4) of WFI diluent batch (b) (4) were not stored under appropriate conditions to prevent potential contamination of the product. It was observed that (b) (4) box lids covering the extra WFI diluent finished product (b) (4) were dislodged and not attached to the boxes potentially exposing the (b) (4) to the environment. Additionally, this (b) (4) was observed to be stored below a (b) (4) unit located within the storage room. Per the firm's Packaging Production Manager, these doses can be distributed and utilized with any lyophilized product the firm manufactures (US and ROW Markets).

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE 	EMPLOYEE(S) NAME AND TITLE (Print or Type) Burnell M. Henry, Investigator Travis S. Bradley, Investigator	DATE ISSUED 09/29/2023
--------------------------	--	---	---------------------------

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER

10903 New Hampshire Avenue, Bldg. 71, Rm 5054
Silver Spring, MD 20993-0002
(240) 402-9160
orabioinspectionalcorrespondence@fda.hhs.gov
Industry Information: www.fda.gov/oc/industry

DATE(S) OF INSPECTION

09/18 - 09/29/2023*

FEI NUMBER

3002972083

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Alain Denis, Site Head

FIRM NAME

Sanofi Pasteur

STREET ADDRESS

1541 Avenue Marcel Merieux

CITY, STATE AND ZIP CODE

Marcy-L'Etoile, Metropole de Lyon, 69280

TYPE OF ESTABLISHMENT INSPECTED

Vaccine Manufacturer

OBSERVATION 4

Laboratory controls do not include the establishment of scientifically sound and appropriate standards designed to assure that drug products conform to appropriate standards of identity, strength, quality, and purity. Specifically, reference standards are not included in analytical sequences to verify (b) (4) control for the following critical test assays.

A. SOP: MLE 1-005714, titled, (b) (4) - A blank is analyzed at the beginning of the (b) (4) method analysis (b) (4) the sample analysis. The (b) (4) absorbance sample result is used for the Purified Vi Polysaccharide bulk (Typhoid Vaccine) (b) (4) content final release assay.

B. SOP: Qu-WIN-0040813, titled, "V16 (b) (4) Use of (b) (4) in Rooms (b) (4) and (b) (4)" - A blank is analyzed (b) (4) method analysis (b) (4) individual (b) (4) samples are analyzed. An average of the (b) (4) readings are used for the (b) (4) (b) (4) measurement. The (b) (4) is measured at the (b) (4) steps during the (b) (4) of the Vi Polysaccharide ((Typhim Vi Vaccine) manufacturing process to (b) (4) for further processing. These steps are identified as critical processing parameters (CPP) in the manufacturing process.

OBSERVATION 5

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not followed. Specifically,

While observing sterile (b) (4) operations for Imovax Rabies batch X1C16 (US Market) on (b) (4) line (b) (4) within the (b) (4) manufacturing building on September 25, 2023, it was observed that (b) (4) operators observed within the Grade (b) (4) supporting area on the (b) (4) line (directly outside the (b) (4)) did not utilize aseptic best practices to limit disruption of (b) (4). It was observed that (b) (4) operators were routinely swaying their hands by their sides while walking throughout the supporting area during (b) (4) in a non-deliberate manner.

SEE
REVERSE
OF THIS
PAGE

EMPLOYEE(S) SIGNATURE

/S/

EMPLOYEE(S) NAME AND TITLE (Print or Type)

Burnell M. Henry, Investigator
Travis S. Bradley, Investigator

DATE ISSUED

09/29/2023

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER

10903 New Hampshire Avenue, Bldg. 71, Rm 5054
Silver Spring, MD 20993-0002
(240) 402-9160
orabioinspectionalcorrespondence@fda.hhs.gov
Industry Information: www.fda.gov/oc/industry

DATE(S) OF INSPECTION

09/18 - 09/29/2023*

FEI NUMBER

3002972083

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Alain Denis, Site Head

FIRM NAME

Sanofi Pasteur

STREET ADDRESS

1541 Avenue Marcel Merieux

CITY, STATE AND ZIP CODE

Marcy-L'Etoile, Metropole de Lyon, 69280

TYPE OF ESTABLISHMENT INSPECTED

Vaccine Manufacturer

*DATES OF INSPECTION

9/18/2023(Mon), 9/19/2023(Tue), 9/20/2023(Wed), 9/21/2023(Thu), 9/22/2023(Fri), 9/25/2023(Mon),
9/26/2023(Tue), 9/27/2023 (Wed), 9/28/2023(Thu), 9/29/2023(Fri)

SEE
REVERSE
OF THIS
PAGE

EMPLOYEE(S) SIGNATURE

/S/

EMPLOYEE(S) NAME AND TITLE (Print or Type)

Burnell M. Henry, Investigator
Travis S. Bradley, Investigator

DATE ISSUED

09/29/2023

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."