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

Use this check box to generate the required 483 statement on page 1 for medical device observations. ☐

| DISTRICT OFFICE ADDRESS AND PHONE NUMBER | DATE(S) OF INSPECTION |
|---|---|
| Christopher Downey, Ph.D., Director of Division of Biotechnology Manufacturing<br>US Food & Drug Administration, Office of Pharmaceutical Quality-OPMA-DBM<br>10903 New Hampshire Avenue, Bldg. 22, Silver Spring, Maryland 20993<br>OPFBLAInspection483Responses@fda.hhs.gov<br>Industry Information: www.fda.gov/oc/industry | 10/17-21/2022<br>FEI NUMBER<br>1819470 MShanks 10/21/2022 |

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Matt Edwards, Vice President-Indianapolis Parenteral Operations (edwards_david_m@lilly.com)

| FIRM NAME | STREET ADDRESS |
|---|---|
| Eli Lilly and Company | Lilly Technology Center 1555 South Harding Street |
| CITY, STATE AND ZIP CODE | TYPE OF ESTABLISHMENT INSPECTED |
| Indianapolis, Indiana 46225 | 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

Your firm's aseptic technique in the (b) (4) drug product filling operations is deficient. During RABS (b) (4) setup activities for both the (b) (4) Filling Line and the (b) (4) (b) (4) Filling Line, the following was observed:

A. Production operators conducted Grade A RABS setup operations partially over unprotected sterile surfaces of components for the stopper or (b) (4) systems.

B. Production operators handled unprotected sterile components (such as the stopper (b) (4) transfer/placement device components) using sanitized (b) (4) instead of handling protective wrapped components that may introduce contaminants onto sterile surfaces in first air zones of the drug product filling area. Operators were also observed sanitizing the entire length of the sterile forceps and other critical sterile surfaces.

C. (b) (4) production operators were observed handling common items (such as the (b) (4) dispenser) interchangeably during Grade A RABS (b) (4) setup interventions.

D. Production operators responsible for sanitizing the filling line's RABS (b) (4) them after RABS (b) (4) operations did not always use an unsoiled surface of the (b) (4) wipe. The activity of using a soiled surface of the (b) (4) wipe was also observed for other items during setup activities.

E. Production operators did not always adhere to (b) (4) (b) (4) during setup and filling activities as described in General Aseptic Practices and Techniques for Parenteral Filling and Manufacturing Operations, Document 001-005056/PRD-95744, version: 27.0, effective date: 10 Oct 2022.

| SEE REVERSE OF THIS PAGE | EMPLOYEE(S) SIGNATURE | EMPLOYEE(S) NAME AND TITLE (*Print or Type*) | DATE ISSUED |
|---|---|---|---|
| | Michael R. Shanks -S (Digitally signed by Michael R. Shanks -S Date: 2022.10.21 15:29:42 -04'00')<br>Nailing Zhang -S (Digitally signed by Nailing Zhang -S Date: 2022.10.21 15:33:37 -04'00')<br>Mercy A. Oyugi -S (Digitally signed by Mercy A. Oyugi -S Date: 2022.10.21 15:31:07 -04'00')<br>Joseph A. Piechocki Jr -S (Digitally signed by Joseph A. Piechocki Jr -S Date: 2022.10.21 15:34:43 -04'00') | Joseph Piechocki, Consumer Safety Officer<br>Nailing Zhang, Lead Interdisciplinary Scientist<br>Mercy Oyugi, Staff Fellow<br>Michael R. Shanks, Senior Biologist | 10/21/2022 |

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| | FEI NUMBER<br>1819 |

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Matt Edwards, Vice President-Indianapolis Parenteral Operations (edwards_david_m@lilly.com)

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| Eli Lilly and Company | Lilly Technology Center 1555 South Harding Street |
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| Indianapolis, Indiana 46225 | Manufacturer |

OBSERVATION 2

Aseptic processing areas for both the (b) (4) Filling Line and the (b) (4) Filling Line are deficient regarding the process for personnel monitoring following critical RABS (b) (4) activities.

Specifically, following critical activities involving RABS (b) (4) interventions and prior to (b) (4) monitoring, production operators would, either sanitize their (b) (4) directly with (b) (4) and/or indirectly sanitize (b) (4) with (b) (4) wipes while sanitizing the (b) (4). This act of exposing their (b) (4) always occurred prior to the monitoring of their (b) (4) for critical RABS (b) (4) interventions.

OBSERVATION 3

Your firm's efficacy study's (Summary of Agent Efficacy Studies to Support Indy Parenteral Manufacturing Site – 2018, Document SAV 000 099/PRT-190127, version: 2.0, effective date: 08 Apr 2022) method for disinfecting using (b) (4) does not adequately support the use and sanitization procedure observed during the setup and production activities of (b) (4) drug product filling operations for both the (b) (4) Filling Line and the (b) (4) Filling Line.

| SEE REVERSE OF THIS PAGE | EMPLOYEE(S) SIGNATURE | EMPLOYEE(S) NAME AND TITLE (*Print or Type*) | DATE ISSUED |
|---|---|---|---|
| | Michael R. Shanks -S<br>Nailing Zhang -S Digitally signed by Nailing Zhang -S Date: 2022.10.21 15:32:48 -04'00'<br>Mercy A. Oyugi -S Digitally signed by Mercy A. Oyugi -S Date: 2022.10.21 15:31:42 -04'00'<br>Joseph A. Piechocki Jr -S Digitally signed by Joseph A. Piechocki Jr -S Date: 2022.10.21 15:35:30 -04'00' | Joseph Piechocki, Consumer Safety Officer<br>Nailing Zhang, Lead Interdisciplinary Scientist<br>Mercy Oyugi, Staff Fellow<br>Michael R. Shanks, Senior Biologist | 10/21/2022 |