DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
550 West Jackson Blvd., 15th Floor Chicago, IL 60661 (312) 353-5863	11/27/2017 – 12/15/2017* FEI NUMBER 3009751352

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Blanca O. Jordan, Site Director

FIRM NAME	STREET ADDRESS
AbbVie, Inc.	1 N. Waukegan Rd.
CITY, STATE, ZIP CODE, COUNTRY North Chicago, IL 60064	TYPE ESTABLISHMENT INSPECTED Human 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 I OBSERVED:

OBSERVATION 1

Procedures describing the handling of written and oral complaints related to drug products are deficiently written.

Specifically,

Your complaint procedures/practices are inadequate for numerous reasons. For example, you are not required to procure complaint samples or test retain samples in the event of death. This issue as well as others are illustrated by the following examples.

A. The following complaints for List 3346 for Lupron 22.5mg/3 month Depot/Pre-filled Dual Syringe (PDS) Kits and List 3473 for Lupron 45mg/6 month Depot/ Pre-filled Dual Syringe (PDS) Kits were not thoroughly investigated for complaints associated with deaths and with leaking. For List 3346 for Lupron 22.5mg/3 month Depot/Pre-filled Dual Syringe (PDS) Kits there were 3 complaints of deaths out of approximately 12 total death complaints for all Lupron products from 12/2015 through 11/2017. List 3473 for Lupron 45mg/6 month Depot/ Pre-filled Dual Syringe (PDS) Kits there were approximately 187 complaints of leaking out of approximately 1,070 total leaking complaints for all Lupron products from 12/2015 through 11/2017.

For the following complaints, there is no documentation regarding the following: an evaluation of complaints to determine if there are similar lot numbers for the same type of complaints for Lupron; an

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evaluation of complaints to determine if there are similar complaints for different strengths of Lupron; no evaluation of the reserve sample when the complaint is for death; no combined evaluation between the manufacturer of the syringes and the packager (AbbVie Inc.) to determine a potential root cause for deaths and leaking.

1. Complaint Record Number 968528 for complaint of death, List 3346 for Lupron Depot 3 month/22.5mg Pre-filled Dual Syringe (PDS) Kits, Batch # (b) (4) , expiration date 2/22/19.

2. Complaint Record Number 912091 for complaint of death, List 3473 for Lupron Depot 6 month /45mg Pre-filled Dual Syringe (PDS) Kits, Batch # (b) (4) Expiration date 10/16/17.

3. Complaint Record Number 923776 for complaint of difficult/unable to use syringe, List 3641 for Lupron Depot 3.75mg Pre-filled Dual Syringe (PDS) Kits, Batch # (b) (4) expiration date 3/8/19.

4. Complaint Record Number 874376 for complaint of needle stick injury, List 3683 for Lupron Depot 4 month/30mg Pre-filled Dual Syringe (PDS) Kits, Batch #(b) (4) expiration date 11/17/18.

5. Complaint Record Number 1107155 for complaint of syringe leaking, List 3346 for Lupron Depot 3 month/22.5mg Pre-filled Dual Syringe (PDS) Kits, Batch (b) (4) , expiration date 2/25/20.

B. Your Duopa Complaint SOP does not require you to review retain samples for leaking complaints. This issue affects Duopa Intestinal Gel, 20mg/ml, application #N203952.

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C. Your SOP QPP07-01-005 "Complaint Closure and Summary" documents you will reply to the complainants if requested. Consequently, you do not respond to your complainants for the majority of the complaints you receive.

D. Your SOP no. 001722201 "Complaint Investigations" gives you a target date of (b) (4) days to complete the child investigation for your complaints received. On 6/28/16 you received a complaint from a Pharmacist documented in complaint no. 880156 for Kaletra lot no. 105672 which was reported to have the expiration date on the bottle worn off. This report documents you did not begin your investigation into this complaint until 8/15/16.

In addition, your investigation into this complaint did not include your review of lots of product manufactured before or after this suspect lot.

E. Complaint Record Reports for all complaints do not include Historical Data Search information for the lot in question. For example, five complaints received which reported "death" did not include information for previous complaints received for that reason which had been reported from 8 to 11 different times on each lot. These products included Humira (Adalimumab) syringe and Venclexta (ventoclax) Tablets products.

OBSERVATION 2
Reserve samples from representative sample lots or batches of drug products selected by acceptable statistical procedures are not examined visually at least once a year for evidence of deterioration.

Specifically,

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A. The following examples from the logbook for Visual Examination of Reserve Samples for Lupron only include documentation of a "Yes" or "No" response for signs of deterioration for the batches of Lupron checked during the annual reserve sample examination for the period of 3/1/2016 to 2/28/2017.

1. Leuprolide Acetate, 6 month, 45mg syringe, PDS Kit, List 3473.
2. Lupron Depot, 3.75mg syringe, PDS Kit, List 3641.
3. Lupron Depot, 3 month, 22.5mg syringe, PDS Kit, List 3346.

B. In addition to the above example, you also do not require a comprehensive listing of defect types in your retain SOP. These issues affect all products you are responsible for reviewing in your retain program.

OBSERVATION 3

Investigations of a failure of a batch or any of its components to meet any of its specifications did not extend to other batches of the same drug product or/and other drug products that may have been associated with the specific failure or discrepancy.

Specifically,

1. Your Exception Report no. 1122859 documents a 24-month fill volume stability failure for Ultane Inhalation (Sevoflurane) 250 mL lot number (b) (4) . During your review of this stability failure you did not evaluate the Ultane batch(es) manufactured immediately before lot (b) (4) as a part of your investigation.
2. Complaint no. 1026806 was opened on May 26, 2017 after receiving a complaint on (b) (4) (b) (4) Capsules lot (b) (4) for bottles which contained faint and broken print,

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which you classify as a (b) (4) defect, along with bottles which were reported to have stains and damage. While you state in your conclusion section "the complaint defect is not likely to be distributed throughout the lot, affect other portions of the lot, or affect other lots to this product" you do not conduct an evaluation of your retain samples packaged before or after this affected lot.

3. Complaint no. 925906 was opened on Nov. 17, 2016 for a lot of Kalentra (Lopinavir/Ritonavir) 20mg/50 mg 120 tablet bottle which reported the expiration date on the label was illegible. As a part of your investigation into this complaint you did not evaluate the lots of product manufactured before or after the affected lot.

OBSERVATION 4
Written production and process control procedures are not followed in the execution of production and process control functions.

Specifically,

Exception Report no. 809450 was opened on March 14, 2016 for a (b) (4) Line Clearance Event – Depakote List 3826-04-13, Batch (b) (4) ". This report documents an event occurred on (b) (4) Zone (b) (4) on March 11, 2016 16 at approximately 0850 when a (b) (4) capsule was identified on the floor in Zone (b) (4) near the support leg of the bottle labeler. Prior to this lot of Depakote there had been (b) (4) lots of (b) (4) tablets packaged, (b) (4) , delayed Release Cap lot (b) (4) and (b) (4) (b) (4) lot (b) (4) packaged before (b) (4) delayed release capsules were packaged on this line on 3/1/2016.

Additionally, your report does not include information on all lots packaged and you did not initiate corrective and preventive actions after becoming aware of this event. [