DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
US FOOD AND DRUG ADMINISTRATION ORA OPQO HQ, (Room # 2032) 12420 Parklawn Drive, Rockville, MD 20857 (ORAPharmInternational483responses@fda.hhs.gov) Industry Information: www.fda.gov/oc/industry	July 28-August 1, 2019 FEI NUMBER 3005202697

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Ofer Ekbali, General Manager Teva Jerusalem OSD Site

FIRM NAME	STREET ADDRESS
Teva Pharmaceutical Industries Ltd.	20 Kiryat Hamada Street, Har Hotzvim Industrial Area
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Jerusalem, Israel	Manufacturer of Drug Products

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DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

QUALITY SYSTEM

OBSERVATION 1

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

1. SOP#00197 v13.0, Handling Complaints, does not always ensure that complaints received on site are documented , processed and investigated in a standardized manner and in compliance with applicable regulations. For example:

a. Complaints reporting the potential lack of effect defect with an assignable lot number do not include consistent evaluation by QC testing on reserve samples unless approved by QA or if a signal trend is identified (after the fourth complaint for the same lot, regardless of the time since the first event).

b. Visual (non-destructive) inspection on reserve samples conducted for all complaints with assignable lot number is conducted only on a portion of the reserve sample without documented justification. SFORM02041 used to document this inspection does not include complete information of units evaluated, elements evaluated by category or include specific references/specifications used.

c. Attempts made to obtain complaint samples are not consistently executed to ensure all possible information is obtained during the investigation. Two attempts to obtain samples are conducted for all complaints, but complaints that "could lead to regulatory issues" include three attempts.

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	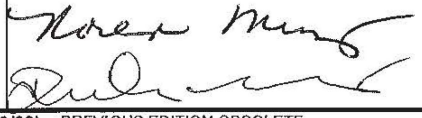	Noreen Muniz, Consumer Safety Officer Dandan Wang, Chemist	08/01/2019

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OBSERVATION 2

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

1. SOP01193v .5.0, Trending of Product Complaints, established on site for trending product quality complaint data to allow early detection and evaluation of impact to product's safety and efficacy is not always followed to ensure timely evaluation of potential complaint trends by lot/defect. The procedure states trend review must be completed within (b) (4) with the investigation report within (b) (4) Records reviewed on site for reported complaint trends disclosed the following investigations opened over (b) (4) :

a. Inv#739549, Opened 23Aug2017-Closed 04 Jul2019, Lot Level Trend Defective Tablets for (b) (4)
Lot #(b) (4)
b. Inv.#831702, Opened 29 Nov 2017 -Closed 31 Jan 2019, Lot Level Trend Incorrect Quantity/Volume (b) (4) Lot (b) (4)
c. Inv #626387, 19Apr2017 -Closed 28 Jul2019 ; Lot level trend for Defective Tablets (b) (4) Tablet Lot (b) (4)

2. Investigations conducted and documented for manufacturing events as described in SOP00099v18.0 Manufacturing Deviation Report, are not always documented to support conclusions reported. For example:

a. Inv#838736, 06Dec2017, Foreign Metallic Particles found during tablet compression of (b) (4) Tab Lost (b) (4) The investigation describes the root cause as incorrect assembly of the compression machine and describes destruction of six (6) containers of the batch. Evidence for containers rejected vs approved was not included with the investigation or with the executed batch record as reviewed during this inspection. The remaining portion of the batch was released.

b. Inv#1286877, 28Apr2019, Open to investigate failure to conduct the annual Microbial test in (b) (4) mg due to skip lot test identified the lack of documents or guidelines on site to ensure that the established frequency for testing (b) (4) was followed but no additional actions were initiated to prevent the recurrence of the event.

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PRODUCTION CONTROLS

OBSERVATION 3

Written production and process control procedures are not followed in the execution of production and process control functions or documented at the time of performance. Specifically,

1. SOP01444 ver10.0, Work Control in the Tableting /Encapsulation Department, allows employees (without justification) to shred documents, un-needed printouts, labels and other articles while conducting work procedures described during compression /encapsulation activities (section 4.1.3.5,English Version of SOP).

2. Appearance inspections conducted during routine manufacturing operations for tablet compression and (b) (4) and capsule filling operations as described in approved procedures SOP01444 ver10.0, Work Control in the Tableting /Encapsulation Department and SOP 014445 v7.0,Working in the (b) (4) Department (b) Plant, Jerusalem Site, do not ensure acceptance criteria is met throughout the process. As described in applicable procedures , the appearance of the tablet /capsule is verified against the written description included with the batch record, but a visual depiction of tablets has never been provided to operators (during training or otherwise) to ensure that deviations or conformance with specifications would be accurately reported for products with visible variations in color and or shape (ex: (b) (4)

In addition, inspections completed during the packaging process as described in TSI00158, Packaging Visual Inspection (b) (4) Plant-Jerusalem, are not fully documented when executed in respective executed packaging batch records as the criteria for inspection (on applicable procedures) does not match reported fields in batch record or ensure detailed inspections are documented. In addition, visual inspection activities are conducted to confirm the identification of product being packaged, but area employees have never been provided any reference (visual depiction) of what acceptable products should look like.

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3. OPI00485 v.14, (b) (4) Testing Unit for Tablets, Capsules, (b) (4) Tablets (b) (4) Plant describes the instructions for operation of the instrument during automatic execution of In-Process Control (IPC) tests on tablets as described during this inspection. The document does not include description or limits for instrument's speed during testing to ensure tablets are consistently loaded and tested and describes activities to be conducted for data back-up by users (not by System or Equipment Administrators).

4 . Activities reported as executed in manufacturing batch records do not always include complete instructions for performance or accurate identification of individual performing reported activities. For example, description of accurate steps conducted for the in-process tests of tablets (as per SOP01444 ver10.0, Work Control in the Tableting /Encapsulation Department) are conducted via automated Tablet Tester (b) (4) but described as conducted manually by operators. The batch record does not include clear and direct instructions on how to report the data obtained from the automatic tester (b) (4) (which describes target ranges as (b) " or (b) (4)). In addition, calculations made to obtain (b) (4) test results included with the batch record are not included.

EQUIPMENT & FACILTIES

OBSERVATION 4

Written procedures for cleaning and maintenance fail to include assignment of responsibility, description in sufficient detail of methods, equipment and materials used or parameters relevant to the operation. Specifically,

1. SOP00043 v16.0, Operating Procedure of the Control Room (b) (4) Jerusalem Site, does not define procedures (as established) to ensure suitable responses for information obtained from the Control System during monitoring of HVAC systems, water systems, storage room's temperature monitoring systems, (b) (4) and energy systems. The procedure fails to detail activities (described during this inspection) for (b) (4) review of alarms in production rooms or activities conducted at the Control Room for monitoring alarms reported but that are not always available or visible at respective production areas for immediate action. The procedure does not describe the reported practice of issuance of a (b) (4) report for each system monitored automatically and steps conducted for the review of alarms reported and actions needed, if any.

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2. SOP00146 v12.0, Monitoring (b) (4) Systems, established on site to define the method for monitoring the quality of the (b) (4) used in the manufacture of drug products fails to describe accurate location of sampling points by room(as (b) (4) points may be available) and does not include accurate description an purpose of all the forms required for documentation of sampling activities as described during this inspection. A visit to the manufacturing areas conducted during this inspection disclosed that sampling points are not identified (associated sampling valves are identified- but are not directly used to take the sample by point) and sampling points reported as not-active were not identified as so.

3. Buildings and facilities used in the manufacture, processing or holding of a drug products do not have the suitable construction or location for facilitate cleaning, maintenance and proper operations. A visit conducted to the manufacturing areas disclosed inadequate (b) (4) systems at the gowning room (leading to manufacturing hallways) and at least 2 doors in (b) (4) rooms ((b) (4) floor). Yellow stains were also observed in sections of the floor in some of the hallways that were described as oil leaks from pallet lifters.

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