DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10903 New Hampshire Avenue, Bldg 51, Rm 4225 Silver Spring, MD 20993 Phone: (301)-796-3334 Fax: (301)-847-8738 Industry Information: www.fda.gov/oc/industry	04/13-17/2015
	FEI NUMBER 1000603876

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Yu Meng, Site Leader, Dalian

FIRM NAME	STREET ADDRESS
Pfizer Pharmaceuticals Limited	No 22, Daqing Road, Economic & Technical Development Zone
CITY, STATE AND ZIP CODE Dalian, Liaoning, 116600 CHINA	TYPE OF ESTABLISHMENT INSPECTED Finished Drug Product Manufacturer

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

OBSERVATION 1

Laboratory control procedures are not followed.

Specifically, during our review of your firm's Quality Control laboratory electronic chromatography data, we identified significant deviations from your written laboratory control procedures. Our review found that when results found to be failing "internal limits" and/or otherwise undesirable/suspect are encountered during analysis of drug products, samples are re-tested until passing/desirable results are achieved. The original test results are not reported, and no laboratory investigation is initiated as required per section 4 of SOP-56980 "Out-of-Specification Result of Chemical and Physical Testing Investigation".

Additionally, trial sample analyses are performed prior to the start of the reported sample analysis. The results of these trial sample analyses are not reported, and were found to differ significantly from the subsequent reported results.

For example:

1) HPLC

A) (b) (4) tablets (b) (4) ng batch # (b) (4) assay via HPLC

- The original analysis was performed on 12/15/14 starting at 11:08pm
  - The result for aliquot #2 was found to fail the internal limit specification of (b) (4) % to (b) (4) % at (b) (4) %
  - These results were not reported, and no investigation was initiated

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	Arsen Karapetyan	Peter E. Baker, Investigator Arsen Karapetyan, Investigator	04/17/2015

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- A set of two unreported sample trial injections for aliquot #2 was then performed on 12/16/14 starting at 7:50am
  - These results appear to confirm the out of limit results

- The sample was then retested on 12/16/14 starting at 10:14am
  - The result for aliquot #2 was found to be within the limit at (b) (4) %
  - These results were reported

B) (b) (4) tablets batch # (b) (4) assay via HPLC

- The original analysis was performed on 12/18/14 starting at 6:38pm
  - According to the Analyst, the result was found to be "unusually high" at (b) (4) % label claim
  - These results were not reported, and no investigation was initiated

- A set of two unreported sample trial injections was then performed on 12/19/14 starting at 7:38am
  - These results appear to confirm the "unusually high" result

- A third unreported sample trial injection was then performed from a different vial position on 12/19/14 starting at 8:10am
  - This result was found to have a significantly lower area response ((b) (4) area counts / (b) (4) % label claim)

- The sample was then retested on 12/19/14 starting at 8:21am
  - The result was found to be (b) (4) %
  - This result was reported

C) (b) (4) tablets batch # (b) (4) content uniformity via HPLC

- The original analysis was performed on 11/25/14 starting at 4:26pm
  - According to the Analyst, the result for tablet #6 found to be "unusually high" at (b) (4) % label claim (vial position (b) (4)
  - These results were not reported, and no investigation was initiated

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- A set of two unreported sample trial injections was then performed on 11/26/14 starting at 7:44am from vial position (b)(4)
  - These results were found to have a lower area response (~(b)(4) area counts)

- The sample was then retested on 11/26/14 starting at 8:19am
  - The area count result for tablet #6 (vial position (b)(4) was found to be (b)(4) (b)(4) % label claim)
  - These results were reported

D) (b)(4) tablets (b)(4) mg batch # (b)(4) related substances via HPLC

- An unreported sample trial injection was performed on 10/13/14 starting at 2:29pm
  - This result was not reported

- The official/reported sample analysis was then initiated on 10/13/14 starting at 7:22pm
  - Our comparison of the trial (unreported) and official (reported) impurities chromatograms found different impurity peak results

2) UV-Vis

A) (b)(4) capsules (b)(4) mg stability batch # (b)(4) (b)(4) - 30C/65%RH) dissolution via UV

- The first analysis was performed on 06/04/2013 at 4:14pm
  - The results from these six tablets was found to be (b)(4) % to (b)(4) % (ave = (b)(4) %)
  - The specification states that no tablet may be less than (b)(4) %
  - These results were not reported, and no investigation was initiated

- The samples were retested on 06/04/2013 at 4:34pm
  - The results from these six tablets was found to be (b)(4) % to (b)(4) % (ave = (b)(4) %)
  - These results were reported

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B) (b)(4) tablets (b)(4) mg stability batch # (b)(4) (b)(4) - 30C/65%RH) dissolution via UV

- The first analysis was performed on 06/24/2013 at 12:58pm
  - The results from these six tablets was found to be (b)(4) % to (b)(4) % (ave = (b)(4) %)
  - The specification states that no tablet may be less than (b)(4) %
  - These results were not reported, and no investigation was initiated

- The samples were retested on 06/28/2013 at 4:44pm
  - The results from these six tablets was found to be (b)(4) % to (b)(4) % (ave = (b)(4) %)
  - These results were reported

OBSERVATION 2

Batch production and control records for each batch of drug product produced do not include an accurate reproduction of the appropriate master production or control record which was checked for accuracy, dated and signed.

Specifically, during our walk-through inspection of your firm's (b)(4) manufacturing unit on 04/13/2015, we noted the presence of uncontrolled records for a number of manufacturing records purported to be controlled under your document control program outlined in SOP-57333 "Issue of Batch Documents in Dosage Form" among other procedures. A summary of the documents identified during our inspection is as follows:

1) Production Batch Manufacturing Records

A) (b)(4) Tablets (b)(4) mg (b)(4) mg (b)(4) batch # (b)(4)

- A loose executed production batch record (page 8/30) was identified.

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- When the data from this loose record was compared to the official/archived production batch record, the data regarding material batch numbers used during manufacturing did not match.

- A sticky note was placed on the loose record stating that the materials were past expiration/retest date.

B) (b) (4) Tablets (b) (4) ng/(b) (4) ng (b) (4) batch # (b) (4)

- A loose executed production batch record (page 8/30) was identified.

- When the data from this loose record was compared to the official/archived production batch record, the data regarding material batch numbers used during manufacturing did not match.

- A sticky note was placed on the loose record stating that the materials were past expiration/retest date.

C) (b) (4) Tablets (b) (4) ng/(b) (4) ng (b) (4) batch # (b) (4)

- Two loose executed production batch records (page 11/30) were identified.

- When the data from the two loose records were compared to the official/archived production batch record, the data regarding temperature/humidity/pressure conditions experienced during manufacturing did not match.

D) (b) (4) Tablets (b) (4) ng batch # (b) (4)

- Approximately eight loose executed pages for each of these batch numbers (pgs. 18, 19, 20, 21, 22, 28, 30, 31) were identified.

- When the data from these records were compared to the official/archived production batch records, the data regarding the manufacturing yield did not match.

- Our investigation found that the formatting between the loose and archived records did not match, despite both being identified as "revision 04"

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- According to the Quality Unit employee identified on the records, the formatting for a number of steps (e.g. (b) (4) had been altered at some point after the completion of manufacturing outside of the document control procedures, and all records re-printed and re-created as necessary.

E) (b) (4) Tablets (b) (4) ng batch # (b) (4)

- A complete blank production batch record (compression) was identified.

- This batch had been manufactured and the record archived in 09/2013

F) (b) (4) Tablets (b) (4) ng

- Two loose blank pages (pg.22/30) were identified (revision 06).

- No batch number had been stamped on these uncontrolled records.

2) Manufacturing Equipment Use Logbook

A) (b) (4) #SCW-5154WH

- An instrument use logbook documenting the use of this equipment from 09/02/2014 to 04/04/2015 was identified.

- When the data from this logbook was compared to the official logbook, the data for use of this equipment (dates/ times) did not match.

3) Training Records

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A) At least four completed training records were identified.

- According to the Training Coordinator, these events had not been entered into the official PLS record.

- One of the records identified was found to be pre-completed with employee IDs, names, and signatures. However, no training subject, dates/times, or other identifying information was listed.

OBSERVATION 3

Records associated with drug product production and within the retention period for such records, were not made readily available for authorized inspection.

Specifically, during our walk-through inspection of your firm's (b) (4) manufacturing unit on 04/13/2015, we noted the presence of a stack of documentation within room (b) (4) approximately 8 inches high. We entered the room and proceeded with our inspection. Approximately 10 minutes later, upon our return to the location where the stack of documentation was identified, we found that it had been removed. We requested its retrieval, and were brought approximately 1/3 of the original stack. We then requested an interview with the individual responsible for the removal of the documents, and found that he had removed the remaining ~2/3 stack from the manufacturing area and placed them in the upper floor construction/expansion area within a wooden crate. The contents of the documents identified within this stack are described above in Observation 2.

OBSERVATION 4

The quality control unit lacks responsibility to approve all procedures or specifications impacting on the identity, strength, quality, and purity of drug products.

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Specifically, your firm's master batch record document control procedure outlined in SOP-57331 "Preparation, Review, Approval and Management of Master Manufacturing Instructions for Dosage Form" states in section 4.3.2 that the Master Batch Records are to be maintained by the "Production Document Management Team". There are no requirements for Quality Unit oversight of Master Batch Record storage and copying for use in manufacturing in order to ensure executed record instructions are accurate reproductions of the master records.

OBSERVATION 5

Laboratory records are not completed contemporaneously.

Specifically, during our inspection of your firm's (b) (4) QC laboratory on 04/14/2015, we reviewed a number of laboratory worksheets for samples under analysis. Our review found that sample preparation actions are not documented contemporaneously. For example:

1) Environmental/personnel monitoring QC worksheet records from 04/08/2015

- Our review found that all results had been recorded as 0 CFU, however, the date/times the plates had been removed from the incubator were not listed.

- The responsible microbiologist stated that he planned to record the date/time later that afternoon. According to the microbiologist all plates had been read and discarded earlier that day.

2) Sterility QC worksheet record for (b) (4) vial batch (b) (4)

- According to the microbiologist, the sample preparation activities had been completed and the tubes placed in the incubator.

-Our review of the QC worksheet found that the data for time/date of incubation was not listed. According to the

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microbiologist, he planned to enter the information later that afternoon.

OBSERVATION 6

Adequate washing and toilet facilities are not provided.

Specifically, during our inspection of your unit # (b) (4) manufacturing perimeter area on 04/13/2015, we noted the presence of a stand-alone washing and toilet facility approximately 50 yards from the aseptic manufacturing unit that was in significant disrepair. Upon entrance to this facility, we found:

- No hand washing station was provided
- An open pit appeared to be used as a urinal

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