DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Food & Drug Administration CDER/OC/DMPQ/ICT Attn: Alicia Mozzachio 10903 New Hampshire Avenue Bldg. 51 Room 4234 Silver Spring, MD 20993 Phone: (301)-796-3206 Fax: 301-847-8738 Industry Information: www.fda.gov/oc/industry	7/14-18/2014
	FEI NUMBER 3002807297

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Dinesh Siyal, Vice President Commercial and Administration

FIRM NAME	STREET ADDRESS
IPCA Laboratories, Ltd.	P.O. Box No. 33 Village Sejavta
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Ratlam, M.P. India 457 002	Active Pharmaceutical Ingredient 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:

Laboratory Control System

1.) Laboratory control records do not include complete data derived from all tests conducted to ensure compliance with established specifications and standards.

Specifically, during our inspection of your firm's QC Analytical Laboratory, we identified significant deviations from Good Laboratory Practices described in SOP GMP/RTM/QC/04/2006 "Recording & Review of Analytical Results of Samples in Instrument Section".

For example:

Gas Chromatography (GC)

A) (b) (4) Finished API batch # (b) (4) US DMF (b) (4) Process Validation stability timepoint (b) (4) @ 30C/65% RH – Residual Solvent (b) (4)) via GC

- Our review of the GC Audit Trail found that the duplicate sample injections were performed on 06/12/13 @ 5:26am and 5:48am, and the result was reported as (b) (4) % (specification = (b) (4) % - (b) (4) %)
- According to the audit trail, the results were originally processed and printed on 06/12/13 @ 5:31am and 5:45am.
- Our review of the comprehensive audit trail found that on 07/18/13, the time/date setting on the controlling PC was set back to 06/12/13 using the administrator privileges, and the two injection results were re-processed; the resulting printout demonstrating that the result had been integrated on 06/12/13.
- At some point after 07/18/13, the time/date setting on the controlling PC was again set back to 06/12/13, and the two injection results were again re-processed; the resulting printout demonstrating that the result had been integrated on 06/12/13.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Joanne E. King	Peter E. Baker, Investigator Joanne E. King, Investigator	07/18/2014

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Food & Drug Administration CDER OC DMPQ/ICT Attn: Alicia Mozzachio 10903 New Hampshire Avenue Bldg. 51 Room 4234 Silver Spring, MD 20993 Phone: (301)-796-3206 Fax: 301-847-8738 Industry Information: www.fda.gov/oc/industry	7/14-18/2014
	FEI NUMBER 3002807297

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Dinesh Siyal, Vice President Commercial and Administration

FIRM NAME	STREET ADDRESS
IPCA Laboratories, Ltd.	P.O. Box No. 33 Village Sejavta
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Ratlam, M.P. India 457 002	Active Pharmaceutical Ingredient Manufacturer

• Our review of the integration results found that the chromatograms appeared to be integrated in an inconsistent manner for no apparent reason; each result (5 standards and 2 samples) was processed using different parameters despite reproducible chromatography.
• Upon our request, re-integration was performed in a consistent manner on 07/16/14; the result was then calculated as (b)(4) %, which fails the specification limit of (b)(4)% - (b)(4)%.
• According to a QC Analyst, integration parameters are manipulated in order to achieve passing results.

• Additionally, while the controlling PC time/date had been manipulated on 07/18/13, one additional injection was performed; however, due to manipulation of the controlling PC time/date the resulting file indicates that the injection was performed on 06/12/13 @ 7:14am. Due to manipulation of the PC time/date and the use of the Administrator privileges by your Analysts, the fate/reporting of this injection result could not be determined.

B) (b)(4) Finished API batch # (b)(4) - US DMF (b)(4) (b)(4) (2011) Commercial Stability batch 12 months @ 30C/65% RH – Residual Solvent (b)(4) via GC

• Our review of the GC Audit Trail found that the duplicate sample injections were performed on 07/18/13 @ 10:22pm and 10:44pm, and the result was reported as (b)(4) % (specification = (b)(4)% - (b)(4) %)
• Our review of the integration results found that the chromatograms appeared to be integrated in an inconsistent manner for no apparent reason; each result (5 standards and 2 samples) was processed using different parameters despite reproducible chromatography.
• Upon our request, re-integration was performed in a consistent manner on 07/16/14; the result was then calculated as (b)(4) %, which fails the specification limit of (b)(4)% - (b)(4)%.
• According to the responsible analyst, integration parameters are manipulated in order to achieve passing results.

C) (b)(4) Finished API batch # (b)(4) (b)(4) Commercial Stability batch (b)(4) @ 30C/65%RH – Related Substances via GC

• Our review of the GC Audit Trail found that the original sample injection had been performed on 06/04/13 @ 5:20am – this injection result was aborted and deleted from the system and is not available for review
• The sample was re-injected on 06/04/14 @ 5:33am; this result was reported.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	PO JKK	Peter E. Baker, Investigator Joanne E. King, Investigator	07/18/2014

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Food & Drug Administration CDER/OC/DMPQ/ICT Attn: Alicia Mozzachio 10903 New Hampshire Avenue Bldg. 51 Room 4234 Silver Spring, MD 20993 Phone: (301)-796-3206 Fax: 301-847-8738 Industry Information: www.fda.gov/oc/industry	7/14-18/2014 FEI NUMBER 3002807297

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Dinesh Siyal, Vice President Commercial and Administration

FIRM NAME	STREET ADDRESS
IPCA Laboratories, Ltd.	P.O. Box No. 33 Village Sejavta
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Ratlam, M.P. India 457 002	Active Pharmaceutical Ingredient Manufacturer

D) Recovered (b) (4) (solvent raw material) batch # (b) (4) – Assay via GC

- Our review of the GC Audit Trail found that the original standard injection had been performed on 04/06/13 @ 7:44am.
- At 8:06am, a second injection was performed using the same file name. According to the Audit Trail, the Analyst confirmed in the software to "overwrite" the previously collected data file/result.
- Due to the over-writing of the previously collected data file, the original injection result was not available for review.

The four representative examples described above were collected during our limited review of the data collected in June-July of 2013 using instrument #'s 052 and 202 (of (b) (4) total GCs). During our limited review, we identified the practice of:

- Manipulation of the controlling PC time/date setting using the Administrator privileges (sub-point A)
- Manipulation of integration parameters to achieve passing/desirable results (sub-point B)
- Aborting ongoing sample analyses and deleting the resulting raw data files (sub-point C)
- Over-writing previously collected raw data files (sub-point D)

Notably, on 08/10/13, critical deviation #CD/RTM/QA/001/2013 was initiated following an anonymous email sent to QA Management on 08/05/13 alleging "strict violence of 21 CFR part 11" in the "GC section" under "supervision" of management. The email alleges that "there is no control of data in the department" and "data can be delete back date worked, as well as falsification is going on". The email states "Take action as early as possible to overcome with future problems in company before audits."

The resulting investigation into the GC section was completed and closed on 11/27/13, and no instances of the four categories of data manipulation/falsification were reported during your firm's review of the data collected using GC #052 and #202, despite your review of the same data and audit trail records reviewed during our inspection (e.g. July 2013). The conclusion is found to be stating "on assessing the impact of errors in the documentation and the other GMP issues does not possess any risk to the quality, purity, safety and efficacy of the product and patient was never at risk." Your firm's written communication to customers dated 08/29/13 states that

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	PD JK	Peter E. Baker, Investigator Joanne E. King, Investigator	07/18/2014

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Food & Drug Administration CDER/OC/DMPQ/ICT Attn: Alicia Mozzachio 10903 New Hampshire Avenue Bldg. 51 Room 4234 Silver Spring, MD 20993 Phone: (301)-796-3206 Fax: 301-847-8738 Industry Information: www.fda.gov/oc/industry	7/14-18/2014 FEI NUMBER 3002807297

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Dinesh Siyal, Vice President Commercial and Administration

FIRM NAME	STREET ADDRESS
IPCA Laboratories, Ltd.	P.O. Box No. 33 Village Sejavta
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Ratlam, M.P. India 457 002	Active Pharmaceutical Ingredient Manufacturer

"Investigation was initiated and based on review (as on date) review there is no impact & risk on product quality."

High Pressure Liquid Chromatography (HPLC)

E) (b) (4) finished API batch # (b) (4) Commercial Batch Release – Assay via HPLC

- Our review of the HPLC Audit Trail found that standard injection titled #4 had been performed on 07/09/13 @ 12:52am; which was prior to the standard titled #3 performed @ 1:17am.
- However, our review of the QC data package found that the raw data files had been manipulated, as standard injection #3 was purported to have been performed at 00:52am, and standard injection #4 was purported to have been performed at 1:17am.

As part of your critical deviation #CD/RTM/QA/001/2013 described above, the data collected via HPLC was included in "Phase II" of the investigation, which was concluded on 05/03/14. Your firm's review of the same raw data and Audit Trail described above in sub-point E (July 2013) did not identify and investigate this data file discrepancy in order to determine the product impact and method of manipulation (e.g. manipulation of the controlling PC date/time settings using the administrator privileges).

Your firm's Phase II HPLC raw data investigation concluded on 05/03/14 was limited to the data collected during the period July – December 2013. Our limited review of the raw data collected using two (of (b) (4) total) HPLC's during the month of May 2013 (not included in the investigation) found the following discrepancies related to released and distributed finished API's:

F) (b) (4) Finished API batch # (b) (4) Commercial Batch Release – Assay via HPLC

- Our review of the HPLC Audit Trail found that the first sample injection for aliquot #2 was performed on 05/28/13 @ 11:01pm. This result was deleted from the system and was not available for review.
- The second sample injection for aliquot #2 was performed on 05/28/13 @ 11:10pm; this result was reported

G) (b) (4) Finished API batch # (b) (4) Commercial Batch Release – Assay via HPLC

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Peter E. Baker, Investigator Joanne E. King, Investigator	07/18/2014

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Food & Drug Administration CDER/OC/DMPQ/ICT Attn: Alicia Mozzachio 10903 New Hampshire Avenue Bldg. 51 Room 4234 Silver Spring, MD 20993 Phone: (301)-796-3206 Fax: 301-847-8738 Industry Information: www.fda.gov/oc/industry	7/14-18/2014
	FEI NUMBER 3002807297

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Dinesh Siyal, Vice President Commercial and Administration

FIRM NAME	STREET ADDRESS
IPCA Laboratories, Ltd.	P.O. Box No. 33 Village Sejavta
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Ratlam, M.P. India 457 002	Active Pharmaceutical Ingredient Manufacturer

• Our review of the HPLC Audit Trail found that the first sample injection for aliquot #1 was performed on 05/01/13 @ 1:12pm. This result was deleted from the system and was not available for review.
• The second sample injection for aliquot #1 was performed on 05/11/13 @ 1:33pm; this result was reported

H) (b) (4) Finished API batch # (b) (4) Commercial Batch Release – Related Substances via HPLC

• A total of three injections were performed on 05/11/13 from 5:00am to 6:07am prior to the initiation of the official/reported sample set initiated at 6:19am.
• Our review of the raw data found that only one (second) of the three injections was available for review; the remaining two (first and third) injection results had been deleted from the system and the identity and results of these injections could not be determined.

2.) Laboratory control procedures are not followed and documented at the time of performance.

Specifically,

A) During our inspection of the microbiology laboratory on 07/14/14, we performed an assessment of the various (b) (4) quality and media growth promotion samples purported to be in-progress (incubation) according to the laboratory documentation.

Our assessment found the following discrepancies:

a) (b) (4) Quality

• Our examination of the 30-35C incubation chamber found that 3 of 45 (b) (4) quality samples purported to having been incubated on 07/09/14 were not present:

o IBP IX SP01
o IBP II DMWPL1302/C1-2 VI/UP01
o IBP XXI SP01 (only 1 of 2 plates was available)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	PD JKK	Peter E. Baker, Investigator Joanne E. King, Investigator	07/18/2014

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Food & Drug Administration CDER/OC/DMPQ/ICT Attn: Alicia Mozzachio 10903 New Hampshire Avenue Bldg. 51 Room 4234 Silver Spring, MD 20993 Phone: (301)-796-3206 Fax: 301-847-8738 Industry Information: www.fda.gov/oc/industry	7/14-18/2014
	FEI NUMBER 3002807297

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Dinesh Siyal, Vice President Commercial and Administration

FIRM NAME	STREET ADDRESS
IPCA Laboratories, Ltd.	P.O. Box No. 33 Village Sejavta
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Ratlam, M.P. India 457 002	Active Pharmaceutical Ingredient Manufacturer

• In an attempt to mask this deficiency, your employee created an additional (falsified) plate for IBP XXI SP01 during our brief exit from the incubation room to make it appear that the sample was complete.

b) Growth Promotion

• Our examination of the 20-25C and 30-35C incubation chambers found that 43 of 117 growth promotion samples purported to having been incubated on 07/09-14/14 were not present.

B) During our inspection of the microbiology laboratory on 07/14/14, we observed two different analysts actively back-dating/falsifying "Temperature Record" logbooks for (b) (4) different refrigerators used to store a variety of cGMP materials. Upon our questioning of one of the analysts on 07/17/14, the analyst stated that she had been "forced" to falsify the record by her direct supervisor.

C) Your (b) (4) Incubator RTM/QC/E-180 kept at temperatures between (b) (4) C and (b) (4) C experienced power outages on 7/10/2014 between 1pm and 2 pm. The Investigation & Impact Assessment Report for this power outage dated 7/10/2014 listed that the incubator was empty. The log book for this incubator listed that on 7/9/2014 (b) (4) for Escherichia coli, and Staphylococcus aureus growth promotion testing were placed into the incubator at 6:55 PM. This growth promotion test requires (b) (4) and (b) (4) respectively to be completed and according to this logbook would have been in the incubator and subject to the temperature excursion caused by the power outage.

3.) Training is not conducted by qualified individuals covering GMP as it relates to the employee's functions.

Specifically, our review of the training history file for your firm's Microbiology "Officer" found that he had not been trained in cGMP as required per SOP GMP/RTM/35/2000 "Training in Current Good Manufacturing Practices", despite working in your Microbiology Laboratory since 05/09/14. According to the Microbiology Manager, this individual was unable to attend the training due to a "heavy workload".

4.) Your laboratory facilities for microbiological monitoring are not adequate to maintain stable incubation conditions for microbiological testing, media growth promotion, and stability studies. Specifically,

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	PD JEK	Peter E. Baker, Investigator Joanne E. Kung, Investigator	07/18/2014

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10903 New Hampshire Ave,Bldg 51,Rm 4225 Silver Springs, MD 20993 (301) 796 3334 Fax:(301) 847 8738 Industry Information: www.fda.gov/oc/industry	10/13/2014 10/17/2014 FEI NUMBER 3007574780

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: V.S.S. Kushwaha, Vice President Technical

FIRM NAME	STREET ADDRESS
Ipca Laboratories LTd	1 Pharma Zone, SEZ Phase II,Sector 3 District Dhar
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Pithampur 454 775, India	Finished Drug Product 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 WE OBSERVED:

OBSERVATION 1

Drug products failing to meet established specifications are not rejected.

Specifically, during our review of your firm's electronic HPLC chromatography data, we noted what appeared to be the laboratory practice of performing sample pre-analysis ("trial") injections prior to initiating the official/reported analyses. These sample pre-analysis "trial" injections are not reviewed and/or reported.

1) Our limited review of randomly selected pre-analysis "trial" unreported sample chromatograms found results that appear to fail your firm's established specifications. No Out-Of-Specification (OOS) investigation was initiated as required per SOP PIT/QAD/059/05 "Procedure for Investigation of Out of Specification Results in Quality Control Laboratory", and no other documentation and/or explanation was provided to describe actions taken to achieve desirable/passing results.

For example:

(b) (4) Tablets USP (b) (4) Assay by HPLC

- The first "trial" sample injection was performed on 01/0 1/13 @ (b) (4)
  - A calculation of this result performed upon our request found the Assay result to be (b) (4) % vs. a specification limit of (b) (4) - (b) (4)
- The second "trial" sample injection was performed on 01/01/13 @ (b) (4)
  - A calculation of this result performed upon our request found the Assay result to be (b) (4) % vs. a specification limit of (b) (4) % - (b) (4)
- The third and fourth (reported/official) sample injections were performed on 01/01/13 @ (b) (4) and (b) (4) respectively.
  - The Assay result for this batch was reported as (b) (4)

2) Our limited review of randomly selected pre-analysis "trial" unreported sample chromatograms also found results that appear to differ significantly from the official/reported results, however, appear to meet your firm's established specifications.

For example:

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Peter E. Baker, Investigator Dipesh K. Shah, Investigator	10/17/2014

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10903 New Hampshire Ave,Bldg 51,Rm 4225 Silver Springs, MD 20993 (301) 796 3334 Fax:(301) 847 8738 Industry Information: www.fda.gov/oc/industry	10/13/2014 10/17/2014 FEI NUMBER 3007574780

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: V.S.S. Kushwaha, Vice President Technical

FIRM NAME	STREET ADDRESS
Ipca Laboratories LTd	1 Pharma Zone, SEZ Phase II,Sector 3 District Dhar
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Pithampur 454 775, India	Finished Drug Product Manufacturer

(b) (4) Tablets USP (b) (4) Assay by HPLC

- The first "trial" sample injection was performed on 01/01/13 @ (b) (4)
  - A calculation of this result performed upon our request found the Assay result to be (b) (4) vs. a specification limit of (b) (4) % - (b) (4)
- The second "trial" sample injection was performed on 01/01/13 @ (b) (4)
  - A calculation of this result performed upon our request found the Assay result to be (b) (4)
- The third "trial" sample injection was performed on 01/01/13 @ (b) (4)
  - A calculation of this result performed upon our request found the Assay result to be (b) (4) %
- The fourth "trial" sample injection was performed on 01/01/13 @ (b) (4)
  - A calculation of this result performed upon our request found ay result to be (b) (4) % vs. a specification limit of (b) (4) % - (b) (4) %
- The fifth and sixth (reported/official) sample injections were performed on 01/01/13 @ (b) (4) and (b) (4) respectively.
  - The Assay result for this batch was reported as (b) (4) %

3) Our limited review of randomly selected pre-analysis "trial" unreported sample chromatograms also found that this practice extends to laboratory investigation processes.

For example:

During our review of the electronic data collected in support of the Out-Of-Specification (OOS) #OOS/030/13/B regarding the content uniformity by HPLC failure for (b) (4) Tablets USP (b) (4) mg (b) (4) we found that prior to the official/reported OOS investigational analyses, pre-analysis "trial" sample injections were performed.

- Prior to the investigational analysis performed by the second analyst on 08/24/13 beginning @ 10:55am, at least one sample trial injection was performed @ 10:39am
  - The Assay result for OOS sample pre-analysis trial was found to be (b) (4) %
  - The average value of the official/reported content uniformity investigation results from this second analyst testing was found to be (b) (4) %

Due to the apparent laboratory practice of directing raw data "trial" chromatogram paths randomly throughout your firm's hard drive in no apparent organized fashion, in what appears to be an attempt to hide results from review, the number of such pre-analysis trial samples performed in relation to each raw material, in-process, and finished drug product analyzed by HPLC at your firm could not be determined.

According to your written procedure PIT/QCD/115/04 "Procedure for Standard Practice in Chromatography", "Trial chromatograms and any other chromatogram (if any) should be attached with relevant documentation and should be stamped with blue color "INVALIDATE" with justification". However, during our review of a representative number of examples,

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Peter E. Baker, Investigator PB Dipesh K. Shah, Investigator DS	10/17/2014

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10903 New Hampshire Ave,Bldg 51,Rm 4225 Silver Springs, MD 20993 (301) 796 3334 Fax:(301) 847 8738 Industry Information: www.fda.gov/oc/industry	10/13/2014 - 10/17/2014 FEI NUMBER 3007574780

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: V.S.S. Kushwaha, Vice President Technical

FIRM NAME	STREET ADDRESS
Ipca Laboratories LTd	1 Pharma Zone, SEZ Phase II,Sector 3 District Dhar
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Pithampur 454 775, India	Finished Drug Product Manufacturer

Including those mentioned above, it appears that "trial chromatograms" are not attached to the QC records and invalidated as required.

OBSERVATION 2

Established laboratory control mechanisms are not followed. Electronic records are used, but they do not meet systems validation requirements to ensure that they are trustworthy, reliable and generally equivalent to paper records.

Specifically,

1) During our review of your firm's electronic GC chromatography data audit trails, we noted what appears to be the laboratory practice of overwriting and deleting raw data files.

For example:

A) (b) (4) Tablets (b) (4) mg (b) (4) by GC

- The first four injections of the sample set were collected on 10/09/13 from 12:12pm to 5:14pm under the sequence titled (b) (4) Tabs (b) (4) mg 09.10.13.seq"
- These four injections were later overwritten and deleted on 10/09/13 starting at (b) (4) using the same sequence and raw data file path
    - As a result, the original chromatogram results are not available for review

B) (b) (4) USP (raw material) (b) (4) by GC

- The first three injections of the sample set were collected on 01/08/14 from 1:51pm to 3:13pm under the sequence titled (b) (4) USP 08.01.14.seq"
- These three injections were later overwritten and deleted on 01/08/14 starting at 4:05pm using the same sequence and raw data file path
    - As a result, the original chromatogram results are not available for review

C) (b) (4) (raw material) method verification for (b) (4) Content by GC

- The first five injections of the sample set were collected on 01/02/14 from 1:24pm to 4:07pm under the sequence titled "System suitability and Method Precision 02.01.14"
- These five injections were later overwritten and deleted on 01/02/14 starting at 5:04pm using the same sequence and raw data file path
    - As a result, the original chromatogram results are not available for review

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Peter E. Baker, Investigator PB Dipesh K. Shah, Investigator DS	10/17/2014

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10903 New Hampshire Ave,Bldg 51,Rm 4225 Silver Springs, MD 20993 (301) 796 3334 Fax:(301) 847 8738 Industry Information: www.fda.gov/oc/industry	10/13/2014 10/17/2014 FEI NUMBER 3007574780

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: V.S.S. Kushwaha, Vice President Technical

FIRM NAME	STREET ADDRESS
Ipca Laboratories LTd	1 Pharma Zone, SEZ Phase II,Sector 3 District Dhar
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Pithampur 454 775, India	Finished Drug Product Manufacturer

D) GC #353 (b) (4) Instrument Calibration

- The calibration sequence was performed and completed on 10/01/12 under the sequence titled "Calibration_Pack column_.seq" (16 total injections)
- The results of this calibration were later overwritten and deleted on 10/03/12 starting at 8:23am using the same sequence and raw data path
  - As a result, the original chromatogram results are not available for review

2) During our review of your firm's electronic FTIR data, we noted duplicate results for the same sample. Our review of the QC data package found that the original result was not included/reported, and no justification was provided regarding the reason for retest.

Additionally, the system audit trail for your (b) (4) FTIR instrument could not be reviewed during our inspection due to software issues.

OBSERVATION 3

Appropriate controls are not exercised over computers or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel.

Specifically, one of your firm's (b) (4) GC instruments (Perkin Elmer #072) is not equipped with a system audit trail that independently records the date and time of actions that create, modify, or delete electronic records.

OBSERVATION 4

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

Specifically, your firm's "Minor" deviation investigation #3015, initiated on 05/02/14 due to:

"Meta data can be deleted in GC (Make - Agilent) and FTIR (Make - Shimadzu) by changing permission from respective instrument user windows login",

did not include:

1) a comprehensive review of the electronic "Meta data", and
2) a product impact evaluation.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Peter E. Baker, Investigator PB Dipesh K. Shah, Investigator DS	10/17/2014

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10903 New Hampshire Ave, Bldg 51, Rm 4225 Silver Springs, MD 20993 (301) 796 3334 Fax:(301) 847 8738 Industry Information: www.fda.gov/oc/industry	10/13/2014 - 10/17/2014
	FEI NUMBER 3007574780

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
TO: V.S.S. Kushwaha, Vice President - Technical

FIRM NAME	STREET ADDRESS
Ipca Laboratories LTd	1 Pharma Zone, SEZ Phase II, Sector 3 District Dhar
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTAB. INVENT. INSPECTED
Pithampur 454 775, India	Finished Drug Product Manufacturer

This deviation investigation was closed on 06/06/14 and found "no impact on the product quality", however, no scientific rationale and/or justification was included to substantiate this claim. Your Quality Representative claims that "the details of the analysis are available in the activity log" (e.g. audit trail), however,

1) one of your firm's (b) (4) GC's does not include an "activity log", and
2) your review of the GC activity log for GC#353 did not identify the systematic deletion of electronic raw data (meta data).

OBSERVATION 5

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

Specifically, during our inspection of the manufacturing unit on 10/14/14, we identified uncontrolled Quality Unit document control stamps within the unlocked In-Process Quality Assurance (IPQA) office located next to the compression and (b) (4) areas. These stamps are used to create QA controlled records printed from the PC located within this office.

There are no written procedures established to control these QA stamps in order to prevent violation of your document control system.

OBSERVATION 6

Employees are not given training in written procedures required by current good manufacturing practice regulations.

Specifically, during our walk-through inspection your manufacturing unit, we identified partially shredded "Training Evaluation" forms for multiple operators that had been completed and signed on 09/23/14 regarding SOP PIT/QAD/019/07 "Procedure for In-process Checks during Tablet Compression/Capsule Filling". We requested and reviewed the official training binders for these operators, and found that the training had been completed on 09/23/14 by your QA Officer, however, no Training Evaluation forms were included as required per section 5.11 of SOP PIT/HRD/003/13 "Procedure for Training of Plant Personnel".

According to the QA Officer who presented the training, he shredded and discarded the Training Evaluation forms for these manufacturing operators "by mistake".

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Peter E. Baker, Investigator PB Dipesh K. Shah, Investigator DS	10/17/2014

interruption at around (b) (4) pm on 10/12/2014, the analyst started another sequence for a retest starting around (b) (4) pm on 10/12/2014.

2) During assay testing for product (b) (4) Tablets USP (b) (4) mg batch numbers (b) (4) and (b) (4) for stability study, the initial duplicate sequence sample injections for sample (b) (4) started around 08/19/2014 a (b) (4) pm, with second injection of sample (b) (4) starting at (b) (4) pm interrupted per your firm's LI/SIL/2014/057 due to "power failure HPLC system went in idle condition" and showing "Incomplete Data". After we verified the data during the inspection, it was observed that the sample injection had partially eluted starting around (b) (4) minutes, with all three injections prior also eluting around (b) (4) minutes. Per your test method, principal peak for (b) (4) is about (b) (4) minutes. Approximately, two days later on 08/21/2014, a new sample solution preparation as performed, and the two batches were retested starting around 1:29 pm with all reported principal peaks eluting at around (b) (4) minutes.

-This discrepancy in your firm's ability to retrieve, review and investigate all electronic raw data is a significant gap in your Data Integrity procedures. Instead of verifying the incomplete data to perform an adequate evaluation of whether the sample solution principal peak eluted or not and its impact on integrity of data, your firm-initiated Laboratory Incident (LI) reports for power failure / instrument failure / computer shut down / stoppage of HPLC system / UPS Power Supply failure / system idle condition and performed retesting of the sample. We reviewed approximately twelve (12) such LI reports, several of which resulted in "Data Missing" or "Incomplete Data". Neither your IQVIA™ or "Project Integrity Failure" assessment reports have investigated the meaning and significance of "Incomplete Data" and "Missing Data" results with respect to integrity of data, in addition to the different type of power interruptions which may cause these interruptions.

OBSERVATION 2

Analyst used (b) (4) with no traceability regarding the (b) (4) reference and no justification was provided for referring (b) (4) " in the method validation protocol and report. This oversight in the method validation was not identified and timely investigated. The method validation report was approved on September 27, 2007.

- Your QC Analysts were using (b) (4) instead of (b) (4) during sample and standard test solutions preparation during (b) (4) step. Your firm has not performed (b) (4) equivalence assessment between (b) (4) and (b) (4) This issue underwent undetected for over 12 years.

2) Your QC Analysts deviated from STPs for over two (2) years while conducting Assay and Related Substances by HPLC tests for (b) (4) Tablets and (b) (4) Tablets. During the inspection, we observed your employees were using (b) (4) other than (b) (4) (b) (4) by deviating from the STPs for over two (2) years or more.

Your Quality Unit failed to identify and investigate Analyst deviation from STPs as one of the potential root causes for Out of Specification (OOS), Out of Trend (OOT), and customer complaints pertaining to lack of effectiveness (see Observation 3A).

C) Your firm's electronic data assessment based on IQVIA™ final report "Forensic Analysis & Electronic Data Assessment", dated 08/17/2018, for chromatographic data systems in response to Warning Letter 320-16-07, dated 01/29/2016 appears to be incomplete. Specifically,

- Your firm's electronic data assessment based on IQVIA™ final report "Forensic Analysis & Electronic Data Assessment", identified some instances, but not all, where interrupted sample injections due to power failure or communication error show that the sample did not run and concluded that the chromatographic data was not available for review. During the current inspection, we demonstrated that

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	8/19/2019-8/23/2019
	FEI NUMBER 3005977675

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Sujit Kumar Rath, Senior General Manager Operations

FIRM NAME	STREET ADDRESS
Ipca Laboratories Limited	Plot No. 65 And 99, Danudyog, Ind. Estate, Piparia
CITY, STATE, ZIP CODE, COUNTRY Silvasa (D And Nh), 396230 India	TYPE ESTABLISHMENT INSPECTED Finished Drug Manufacturer

There is a failure to thoroughly review any unexplained discrepancy and the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

Specifically,

Your firm's OOS and OOT investigations are deficient in that failures were invalidated based on acceptable retest results without identifying the root causes of the original failures. For example:

A) OOS No.: SIL/OOS/2019/022 for Assay by HPLC failure on (b) (4) USP API lo (b) (4) and (b) (4) Your QC Unit invalidated the original test data based on the following rationales:

- Sample and standard test solutions were discarded prior to processing and verifying the analytical test results.
- Sample and standard preparations were ove (b) (4) for stability of solutions.

During the inspection, we observed your firm has not conducted evaluation of solution stability during the method validation and there was no documented evidence provided pertaining to the claim of (b) (4) (b) (4) of solution stability.

The firm compromised the integrity of OOS investigation by changing the HPLC system from HPLC equipment ID: SQC 102 to SQC 101. Additionally, a repeat analysis was performed by preparing fresh sample, standard, mobile phase and diluent solutions that resulted in a passing test result.

B) OOT No.: OOT/QC/SIL/004/18 for Dissolution by UV on (b) (4) Tablets. Your QC Unit invalidated OOT based on the assumption of not (b) (4) prior to (b) (4) the sample solution, which deviated from your STP for Dissolution by UV test. Your QC Analysts used (b) (4) by (b) (4) using a (b) (4) instead of (b) (4) This issue

93893, Change control date created: March 07, 2018, Total days change control open: ~ 523 days;
94270, Change control date created: March 10, 2018, Total days change control open: ~ 520 days;
94709, Change control date created: March 15, 2018, Total days change control open: ~ 515 days;

Additionally, your firm has approximately eighteen (18) additional change controls that are in open status for about 235 to 440 days from year 2018. Additionally, for year 2019, there are about seventy-seven (77) change controls are in open status with the oldest being about 214 days.

- CAPAs open from years 2017 and 2018:

72700, CAPA date opened: June 30, 2017, Total days CAPA open: ~770 days;
90912, CAPA date opened: January 29, 2018, Total days CAPA open: ~561 days;
105293, CAPA date opened: July 14, 2018, Total days CAPA open: ~396 days;
106432, CAPA date opened: July 27, 2018, Total days CAPA open: ~383 days;
110990, CAPA date opened: September 14, 2018, Total days CAPA open: ~336 days;
114529, CAPA date opened: October 26, 2018, Total days CAPA open: ~294 days; and
116375, CAPA date opened: November 22, 2018, Total days CAPA open: ~268 days.

Additionally, your firm has approximately eighty-five (85) CAPAs in open status for year 2019, of which about twenty (20) CAPAs are in open status for over one-hundred (100) days.

C) Your firm's Quality Unit allows the destruction of draft and interim laboratory investigation reports using shredders maintained in your QA office area. The logbook maintained for controlling the destruction of documents showed several entries pertaining to the destruction of interim investigation reports. Additionally, we observed several GMP documents under "Q" drive of QC computers that were not under control of your Quality Unit. The documents stored under "Q" drive contained but not limited to, draft investigation reports, draft SOPs, formats (worksheets) for conducting laboratory investigations, etc. These documents can be deleted, copied and modified by all QC personnel.

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	8/19/2019-8/23/2019
	FEI NUMBER 3005977675

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Mr. Sujit Kumar Rath, Senior General Manager Operations

FIRM NAME	STREET ADDRESS
Ipca Laboratories Limited	Plot No. 65 And 99, Danudyog, Ind. Estate, Piparia
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Silvasa (D And Nh), 396230 India	Finished Drug Manufacturer

Similarly, during our review of your tablet compression equipment machine interface, we observed PDF documents with production results, changes, and alarms encountered for several batch records manufactured in 2014 on the machine interface desktop recycle bin. It was observed that the recycle bin is available without restriction to all production operators during real time compression activities. Additionally, we observed that all raw data generated in your equipment software as a result of tablet compression operations is stored on the machine interface desktop D Drive without restriction, where every production operator can access all the raw data in real time, including those generated by other operators for prior batches. Per your IT, this raw data is backed up (b) (4)

X Pratik S Upadhyay
Generic Drug User Fee Amendments (GDUFA)
Signed By: Pratik S. Upadhyay -S
Date Signed: 08-23-2019 08:42:38

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Arsen Karapetyan, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Generic Drug User Fee Amendments (GDUFA)	X Arsen Karapetyan Investigator - Dedicated Drug Cadre Signed By: Arsen Karapetyan -S Date Signed: 08-23-2019 08:40:55	8/23/2019

AND finally! BUT … it was just Itas … oh, well …..

URL: Intas Pharmaceuticals Limited - 652067 - 07/28/2023 | FDA

1. Your firm's quality control unit failed to exercise its responsibility to ensure drug products manufactured are in compliance with CGMP, and meet established specifications for identity, strength, quality, and purity (21 CFR 211.22).

You failed to ensure reliability of data relating to the quality of medicines produced at your facility. Our inspection revealed serious deviations, including but not limited to, inadequate oversight of original CGMP documents, deficient controls over computerized systems, insufficient laboratory investigations, and aborted chromatographic sequences.

Senior facility managers failed to exercise their authority and responsibility to ensure reliable data, leading to severe data integrity deficiencies in your production and laboratory departments. These findings also indicate that your quality assurance function is not exercising its responsibilities, including but not limited to, oversight and control over the adequacy and reliability of CGMP data used throughout your operation.

A. You failed to assure integrity of analytical testing data. Some examples include:

1. Our investigators observed plastic bags filled with torn and discarded original CGMP documents in your quality control (QC) scrap area under a stairwell, in your general parenteral scrap room, and on a truck outside your facility. Among these CGMP documents were engineering checklists associated with the Environmental Monitoring System (EMS), torn Karl Fischer (KF) analytical test reports, auto titration curves, and analytical balance weight slips for finished drug products.

2. An analyst destroyed CGMP records by pouring acetic acid in a trash bin containing analytical balance slips for testing the standardization of **(b)(4)**. A QC employee stated he observed the same analyst destroy KF titration curves and balance printouts. The employee reported the incident to QC laboratory management on November 22, 2022. An investigation into the destruction of the torn CGMP documents and the impact to your drug product quality was not initiated until November 28, 2022.

Intas Warning Letter - Intas Pharmaceuticals Limited, FEI 3003157498, at Plot No. 457- 458 & 191/218P, Sarkhej - Bavla Highway, Matoda - Sanand, Ahmedabad

URL: Intas Pharmaceuticals Limited - 662868 - 11/21/2023 | FDA

1. Your firm's quality control unit failed to exercise its responsibility to ensure drug products manufactured are in compliance with CGMP, and meet established specifications for identity, strength, quality, and purity (21 CFR 211.22).

Your Quality Assurance (QA) and production departments failed to provide adequate oversight and ensure the reliability of data related to the quality of finished drug products manufactured at your facility. Since 2021, visual inspectors manipulated particle and other defect counts on manual visual inspection records in many instances, in order to keep the finished product batches within rejection limits. More specifically, the investigation found that operators manipulated the defect quantities "to keep the category wise rejections within limits to avoid a deviation and investigation."

In addition, multiple operators manipulated the reported defects, including **(b)(4)** attributes and particle counts, on manual visual inspection records to have identical numbers. This practice was repeatedly performed by at least nine different manual visual inspectors on trays of **(b)(4)**. The records, filled out by multiple operators, had an identical number of defects listed for all drug product defect categories.

Production managers including, but not limited to, front line supervisors failed to ensure reliable data, leading to significant data integrity deficiencies in your production records.

In addition, there was a lack of QA department review and oversight of visual inspection records, and your firm continued this egregious pattern of recording and altering defect counts. These findings indicated that your QA department was not exercising its basic responsibilities including, but not limited to, oversight and control over the adequacy and reliability of all CGMP data at your facility.

In your response, you acknowledge the discrepancies found in the visual inspection records and identify the contributing factors to these deviations as "inadequate data management processes, inadequate training and procedures, and inadequate quality oversight of the visual inspection operation." You state that "all the visual inspectors in this area have been disqualified" and "operators have been moved to the secondary packaging area and are not participating in GMP activities."

NATCO pharma

Record Date	FEI Number	Firm Name	Record Type	Country	Date Posted
10/09-18/2023	3004540906	NATCO Pharma Limited	483	India	11/1/2023

URL: Compliance Document: NATCO Pharma Limited Rangareddy, Telangana, India (fda.gov)

From Obs 2

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Senior Vice President - Operations

FIRM NAME	STREET ADDRESS
India	TYPE ESTABLISHMENT INSPECTED: Sterile and Non-sterile Drug Products Manufacturer

Specifically,

Your Quality Unit lacks an oversight on the control and management of GMP documents that are critical in ensuring the drug products manufactured and tested at your site are safe and effective. For example, on 09-Oct-2023, we observed your Quality Control (QC) Microbiology Laboratory, Production, Engineering and Maintenance department's employees deviated from your SOP No.: GQA/083-1, Titled: Data Integrity Policy, Effective date: 19-Jul-2021 and SOP No.: GQA/027-06, Titled: Good Documentation Practices, Effective date: 10-Nov-2020 by destroying GMP documents by tearing it into pieces and disposing as scrap.

There is also a lack of Quality Unit oversight on employees' practices of documenting GMP data on uncontrolled white paper and later disposing these papers by tearing into pieces inside your firm's main scrapyard. Among multiple sections violated by destroying GMP documents, section 4 of SOP No.: GQA/083-1 and section 7.1 of SOP No.: GQA/027-06 refers to [redacted] principle to ensure integrity of data and Good Documentation Practices. Further, section 7.3 of SOP No.: GQA/027-06 refers to *"All entries shall be made directly on to the original record. Do not use scrap paper."* In the scrapyard we observed torn pieces of analytical weight slips (balance printouts), sterility testing [redacted] printouts, [redacted] operation printouts, BET validation protocol, filter integrity test printouts, and batch manufacturing record page along with manufacturing and testing activities recorded in blue and black color ink ball point pens on uncontrolled white printing papers, tissue papers, notebook pages, and gloves. According to your firm's SOP No.: GQA/001-11, Titled: SOP on SOP, Effective date: 31-Jul-2023, section: 7.2.17 Quality Assurance personnel shall use blue color ink ball point pens for data recording and approval. Cross-function (all other departments including QC, Production, Materials, etc) teams shall use black color ink ball point pens.

Upon putting together some of the torn pieces of documents with the help of your employees, your Quality Unit management stated the torn pieces belonged to original record, raw data and meta data

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Pratik S Upadhyay, Investigator Saleem A Akhtar, Investigator	10/18/2023

FORM FDA 483 (09/08) PREVIOUS EDITION OBSOLETE INSPECTIONAL OBSERVATIONS PAGE 9 of 26 PAGES

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	11/17-21/2014
	FEI NUMBER 3002949085

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: KVSN Raju, Senior Director - Works, Location Head

FIRM NAME	STREET ADDRESS
Dr. Reddy's Laboratories Ltd.	IDA, Pydibhimavaram (Village), Ranasthalam Mandal
CITY, STATE AND ZIP CODE Srikakulam District - 532 409, Andhra Pradesh	TYPE OF ESTABLISHMENT INSPECTED Active Pharmaceutical Ingredient 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

Laboratory control records do not include complete data derived from all tests conducted to ensure compliance with established specifications and standards, including examinations and assays.

Specifically, during our inspection on 11/18/14, we requested a review of archived electronic chromatography data collected during the period 01/2012. Your firm facilitated the review of only 3 out of the (b)(4) analytical chemistry laboratories. The presence of the (b)(4) laboratory facility ("CQC") was only discovered during our review of the HPLC audit trials on 11/20/14, which introduced a significant delay in our ability to perform a comprehensive review of the electronic cGMP chromatography data. No explanation was provided regarding the failure to facilitate the review of cGMP data collected within this "CQC" laboratory.

During our subsequent limited review of the electronic chromatography collected within the "CQC" laboratory during the period 01-02/2012, we noted the following instances where written procedures regarding the raising of laboratory incidents (SOP 01-045/03 "Handling of Incidents") and/or out-of-specification (OOS) investigations (SOP 08-004/12 "Laboratory Investigation of Out of Specification Results") were not followed:

A) (b)(4) batch # (b)(4) Assay/Related Substances by HPLC

- The first sample analysis was performed on 01/14/12 at (b)(4)

- The result for was found to be failing the specification limit (SI/CMAT2-001/02) for known and unknown impurities. The sample preparation and test results were not documented and reported.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Peter E. Baker, Investigator Dipesh Shah, Investigator Dr. Carmelo Rosa, Director DIDQ	11/21/2014

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	11/17-21/2014
	FEI NUMBER 3002949085

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: KVSN Raju, Senior Director - Works, Location Head

FIRM NAME	STREET ADDRESS
Dr. Reddy's Laboratories Ltd.	IDA, Pydibhimavaram (Village), Ranasthalam Mandal
CITY, STATE AND ZIP CODE Srikakulam District - 532 409, Andhra Pradesh	TYPE OF ESTABLISHMENT INSPECTED Active Pharmaceutical Ingredient Manufacturer

- The second injection of this first analysis appeared to contain an extra peak (possibly carryover), and the sample preparation and test results were not documented and reported.

- The reported sample analysis was performed on 02/11/12 starting at (b) (4)

- The sample preparation and test results were recorded on the QC "Record of Analysis" (worksheet), and were reported.

D) (b) (4) batch # (b) (4) Purity by HPLC

- The first sample analysis for preparation #1 was performed on 01/27/12 starting at (b) (4)

- The result was found to be failing the purity specification limit found in S-03-QUE1-01/00 (NLT (b) (4) %) at (b) (4) %, and this test result was not reported.

- The reported result for sample preparation #1 was performed on 01/27/12 starting at (b) (4)

- The result was reported as meeting specifications.

E) (b) (4) batch # (b) (4) stability sample 9 months @ 40C/75% RH Assay/Related Substances by HPLC

- The first sample analysis for preparation #1 was performed on 01/27/12 starting at (b) (4)

- The result for Assay was found to be (b) (4) %, and this result was not reported.

- The reported result for sample preparation #1 was performed on 01/27/12 starting at (b) (4)

- The result was reported as (b) (4) %.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	PB	Peter E. Baker, Investigator Dipesh Shah, Investigator Dr Carmelo Rosa, Director DIDQ	11/21/2014

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	11/17-21/2014
	FEI NUMBER 3002949085
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED TO: KVSN Raju, Senior Director - Works, Location Head	
FIRM NAME Dr. Reddy's Laboratories Ltd.	STREET ADDRESS IDA, Pydibhimavaram (Village), Ranasthalam Mandal
CITY, STATE AND ZIP CODE Srikakulam District - 532 409, Andhra Pradesh	TYPE OF ESTABLISHMENT INSPECTED Active Pharmaceutical Ingredient Manufacturer

OBSERVATION 2

Computerized systems do not have sufficient controls to prevent unauthorized access or changes to data. There are no controls in place to prevent omissions in data.

Specifically, during our inspection of the "PD Laboratory", used as an analytical support laboratory for quality and manufacturing cGMP investigations, we found that each of the (b)(4) HPLCs and (b)(4) GCs currently in use were not equipped with sufficient controls (e.g. audit trails) to prevent changes to or omission of raw data.

Our random review of one HPLC (#AD021) hard drive uncovered evidence that analytical raw data had been collected throughout the month of November 2014 and had been deleted. No hard copy printouts of these results could be provided, the testing was not recorded in the instrument use logbook, and the identity of the product(s) analyzed could not be determined. According to the responsible analyst, another individual had logged into the system using his credentials and had performed injections and deletion without his knowledge.

Additionally, we found that the systems are configured so that no passwords are required during log-in, including the use of the software Administrator privileges.

OBSERVATION 3

Batch production and control records do not include the weights and measures of components used in the course of processing each batch of drug substance produced, and entries are not made directly after performing the activities.

During our inspection of your firm's Manufacturing Office in Production Block (b)(4) (PB (b)(4) on 11/17/2014, we found Manufacturing Batch records AFGH001431, AFGH001755, AFGH002223, AFGH002224, AFGH006464,

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	PB	Peter E. Baker, Investigator Dipesh Shah, Investigator Dr. Carmelo Rosa, Director DIDQ	11/21/2014

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	11/17-21/2014
	FEI NUMBER 3002949085

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: KVSN Raja, Senior Director - Works, Location Head

FIRM NAME	STREET ADDRESS
Dr. Reddy's Laboratories Ltd.	IDA, Pydibhimavaram (Village), Ranasthalam Mandal
CITY, STATE AND ZIP CODE Srikakulam District - 532 409, Andhra Pradesh	TYPE OF ESTABLISHMENT INSPECTED Active Pharmaceutical Ingredient Manufacturer

AFGH006465, AFGH002919 and AFHWS00176 documented without information such as weights, checked by signatures, and material dried specimen product labeling. The manufacturing activities described in these batch records had been completed. According to your QA manager, information such as the Details of Solvent/Water used (Before and After Process), Checked by Signatures and Dates, (b) (4) Drum tare weight (kg), W.E.ID. Number, Net weight, Gross weight, packing loss, and attachment of the Specimen product label needs to be recorded in the Batch Manufacturing Record contemporaneously.

According to section 4.2 of SOP Number 01-018/11, "Preparation, Issue, Filling and Verification of Batch Production Record" states, "Fill up the BPR before starting and after completion of every operation in appropriate column and sign in the BPR".

OBSERVATION 4

Procedures regarding the issuance, revision, superseding, and withdrawal of all documents are not followed.

Specifically, your firm fails to have a document control system to ensure that the issuance, revision, withdrawal of all documents be controlled with maintenance of its revision history.

For example:

A) On 11/17/2014 numerous bags described as waste material were observed in your firm's waste area containing copies of issued/unused batch records, raw data, analytical results, stability summary reports, training records, draft SOPs and controlled documents. In addition, on this same day, Master Batch Records, training records and a significant amount of raw data related to API products produced were observed in employee's personal areas in different areas throughout the manufacturing facility. Although your firm has implemented SAP as the official data/product tracking and disposition system, the inspection found that many critical documents were not controlled and maintained under appropriate custody, aligned with the requirements of your SAP database. In addition, your SOP No. 01-042/03: "Documentation Center-Archival, Retention & Disposition", requires that you maintain your production and testing (GMP documents) for (b) (4) after expiry (for APIs), or (b) (4) for

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Peter E. Baker, Investigator Dipesh Shah, Investigator Dr. Carmelo Rosa, Director DIDQ	11/21/2014

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	11/17-21/2014
	FEI NUMBER 3002949085

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: KVSN Raju, Senior Director - Works, Location Head

FIRM NAME	STREET ADDRESS
Dr. Reddy's Laboratories Ltd.	IDA, Pydibhimavaram (Village), Ranasthalam Mandal
CITY, STATE AND ZIP CODE Srikakulam District - 532 409, Andhra Pradesh	TYPE OF ESTABLISHMENT INSPECTED Active Pharmaceutical Ingredient Manufacturer

not been completed. Five retests were conducted obtaining passing results, which led to your conclusion that the final test result (5th of the 5 retest injection results) would be the final reported result. The investigation remains open, unsigned by the QC unit, and has yet to be assessed by the QA unit.

OBSERVATION 8

The Process Validation approach does not provide documented evidence that the process, operated within established parameters, can perform effectively and reproducibly to produce an intermediate or API meeting its predetermined specifications and quality attributes.

Specifically, your firm fails to adequately validate your API manufacturing processes, and to have scientifically sound sampling plans during your validation. For example,

A) The validation for the following APIs (currently under DMF review): (b) (4) API, (b) (4) API, and (b) (4) API, was justified using the routine sampling and testing processes. This approach provided no assurance of reproducibility at each critical manufacturing process step, and that each critical parameter had been assessed to ensure your APIs can consistently meet the required quality attributes. No scientific justification/rationale was provided regarding the sampling plans used during your validation.

B) A significant number of (b) (4) batches and other APIs are rejected and/or reprocessed. For example, during year 2012, 4 lots of (b) (4) were reprocessed, during year 2013, 18 batches of (b) (4) (b) (4) were reprocessed, and in 2014, 7 lots of (b) (4) were reprocessed.

OBSERVATION 9

Adequate and clean washing and toilet facilities are not provided for personnel.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	PB	Peter E. Baker, Investigator Dipesh Shah, Investigator Dr. Carmelo Rosa, Director DIDQ	11/21/2014

Dr Reddy 483 – Telangana – OCT 2023

URL: Compliance Document: Bachupally, India (fda.gov)

Post may br worth reading: https://www.linkedin.com/posts/johntenglish_fda-drugmanufacturing-tmac-activity-7130319299688189953-gwrP

As a result of finding powdery materials of [redacted] and [redacted] actives in [redacted] drug product, the firm reported Field Alert for [redacted], Batch Number: [redacted], Expiry date: [redacted].

C. The [redacted] non-dedicated Rapid Mixture Granulators (RMGs) used in the manufacturing of finished drug products at the firm have not been cleaned and verified for cleanliness underneath the mounted platform areas since their installation several years ago. There is a potential for deposition of powdery materials and microbial growth in these areas in all RMGs across the facility.

Serial. No.	Equipment name	Equipment number	PQ Date
1.	Rapid Mixer Granulator [redacted] L	[redacted]	[redacted]
2.	Rapid mixing granulator [redacted] L	[redacted]	[redacted]
3.	Rapid mixing granulator [redacted] L	[redacted]	[redacted]
4.	Saizoner Mixer Granulator [redacted] L	[redacted]	[redacted]
5.	Saizoner Mixer Granulator [redacted] L	[redacted]	[redacted]
6.	Rapid mixing granulator [redacted] L	[redacted]	[redacted]
7.	Rapid Mixer Granulator [redacted] L	[redacted]	[redacted]
8.	Rapid mixing granulator [redacted] L	[redacted]	[redacted]
9.	Rapid Mixer Granulator- [redacted] L	[redacted]	[redacted]

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Saleem A Akhtar, Investigator Pratik S Upadhyay, Investigator - Dedicated Drug Cadre	X	DATE ISSUED 10/27/2023

FORM FDA 483 (09/08) PREVIOUS EDITION OBSOLETE INSPECTIONAL OBSERVATIONS PAGE 4 of 23 PAGES

Dr Reddy continued on next page .....

Failure to investigate ….

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Global Head of Quality	
FIRM NAME	STREET ADDRESS
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
India	Drug Manufacturer

There is a failure to thoroughly review any unexplained discrepancy and the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

Specifically, the quality unit failed to investigate deviations and investigations thoroughly that could potentially impact the patient safety and product quality. For example:

A. The firm's Quality Unit did not timely conclude the investigations relating to batch failure and recalled failing batches from the US market. For examples,

The firm's QC unit found failing results for [redacted], Batch Numbers: [redacted] and [redacted], Manufacturing date: [redacted], Expiry date: [redacted], Test: Dissolution by HPLC, Stability timepoint: [redacted] at [redacted]. Upon confirming the failing results at L1 and L2 stages on [redacted] and [redacted]. The firm logged-in a single [redacted] investigation ([redacted] No.: [redacted], date initiated: [redacted]) for both the lots by underreporting the total number of [redacted]. The firm concluded [redacted] investigation for both the lots as "Valid" i.e. failing to meeting specification limit on [redacted]. Further, the firm initiated a separate [redacted] investigation ([redacted] and [redacted]) on [redacted] and filed a Field Alert on [redacted] to the agency. The firm concluded the OOS investigation as "Valid" on [redacted] which is after crossing [redacted] shelf life of the product.

There was no justification provided for the delay of over [redacted] months in concluding the failing test results investigation for these annual stability batches. As a result of delayed investigation, [redacted], Batch Numbers: [redacted] and [redacted] batches remained available for purchase to the US customers and these batches were not recalled from the US market. On [redacted], the firm simply closed FAR without evaluating the impact of

Centaur pharma (India) – Warning letter -Failure to clean for 14yyears? (why not noticed sooner?)

URL: Centaur Pharmaceuticals Private Ltd. - 655231 - 07/25/2023 | FDA

1. Your firm failed to clean, maintain, and, as appropriate for the nature of the drug, sanitize and/or sterilize equipment and utensils at appropriate intervals to prevent malfunctions or contamination that would alter the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements (21 CFR 211.67(a)).

Your cleaning and maintenance procedures for non-dedicated **(b)(4)** equipment **(b)(4)**, including your **(b)(4)** and **(b)(4)**, are inadequate. Our inspection identified residues of what appeared to be different products on direct and indirect product contact surfaces, including those located inside **(b)(4)** systems, **(b)(4)** units **(b)(4)**, and **(b)(4)**. Your firm acknowledged that sections of the **(b)(4)**, **(b)(4)**, and **(b)(4)** have not been cleaned or examined for cleanliness since they were installed over 14 years ago. During the inspection, your analytical testing confirmed these residues contained multiple active ingredients. Furthermore, during the inspection, you collected residue samples at the end of placebo batches and subsequent cleaning, which also demonstrated active ingredient cross-contamination on surfaces.

(b)(4) over dirty surfaces can facilitate contamination of the drug being processed in an **(b)(4)**. Robust design, cleaning, and maintenance of this and other equipment is critical to prevent cross-contamination.

The inspection also noted missing or faulty **(b)(4)** in **(b)(4)**, as well as material back flow, which resulted in equipment contamination. For example, you stated the manually operated **(b)(4)** inside **(b)(4)** number CP/PT/**(b)(4)**-01 in **(b)(4)** Area **(b)(4)** is always in the open position. You also indicated the buildup of powder inside the **(b)(4)** and **(b)(4)** of this equipment was caused by the back flow of materials during equipment **(b)(4)**.

As a result of these inspectional findings, you communicated with your client, Breckenridge Pharmaceutical, Inc., who initiated a recall of numerous batches of alprazolam tablets and clobazam tablets manufactured in your **(b)(4)**. We also acknowledge the recall initiated by **(b)(4)** of **(b)(4)** tablets you manufactured.

Biocon – Malaysia – multiple notes in post below:
https://www.linkedin.com/posts/johntenglish_fda-drugmanufacturing-malaysia-activity-7097053366102450176-Ev4F

For the below 483: Compliance Document: Johor, Malaysia (fda.gov)

FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER
12420 Parklawn Drive, Room 2032
Rockville, MD 20857
ORAPHARMInternational483responses@fda.hhs.gov

DATE(S) OF INSPECTION: 07/10/2023-07/20/2023

FEI NUMBER:

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Senior Vice President & Site Head

FIRM NAME

STREET ADDRESS

CITY, STATE, ZIP CODE, COUNTRY
Malaysia

TYPE ESTABLISHMENT INSPECTED
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 WE OBSERVED:

DRUG

OBSERVATION 1

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

(This is a repeat observation)

A. On 07/10/2023 and 07/12/2023, we inspected the post assembly and/ or aseptic filling of [redacted] ml. batches [redacted] respectively. We observed the following deficiencies.

- Aseptic operators blocked HEPA unidirectional airflow when re-plenishing [redacted] stoppers and [redacted] seals to their respective [redacted].
- Sterile scissors used to cut open [redacted] bags containing sterile components were held in non-sterile holders when not in use.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Eileen A. Liu, Investigator (Lead) Patty P. Kaewussdangkul, Investigator Daniel Lahar, Investigator Rong Guo, Investigator	Eileen A. Liu -S Digitally signed by Eileen A. Liu -S Date: 2023.07.19 20:21:44 -07'00' Patty P. Kaewussdangkul -S Digitally signed by Patty P Kaewussdangkul -S Date: 2023.07.19 20:22:59 -07'00'	07/20/2023

FORM FDA 483 (09/08) PREVIOUS EDITION OBSOLETE INSPECTIONAL OBSERVATIONS PAGE 1 OF 10 PAGES

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	April 1 - 6 & 9, 2013
	FEI NUMBER 3003297374

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Bhailalbhai Nathabhai Patel, Managing Director

FIRM NAME	STREET ADDRESS
Canton Laboratory	110-A & B, GIDC Estate, Makarpura Road
CITY, STATE AND ZIP CODE Vadodara - 390010 India	TYPE OF ESTABLISHMENT INSPECTED API, Excipient & Dietary Supplement 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

Pharmaceutical Observations

OBSERVATION 1

Laboratory records do not include complete data derived from all tests conducted to ensure compliance with established specifications and standards.

Specifically, the quality control unit does not have raw data related to analyses. For example,

a. There is no microbiology data and no evidence to indicate that any microbiological analysis was performed prior to the release of batches (b) (4) and (b) (4) of (b) (4) USP. The Certificates of Analysis for these batches indicate passing results for Staphylococcus aureus and Pseudomonas aeruginosa, even though these batches were not analyzed for the potential presence of these organisms. A review of the sample log book maintained by the microbiology section for analyzed samples found that there are no entries for samples of these batches.

b. There is no raw data for any of the tests for metallic impurities performed by the QC laboratory for raw materials, in-process materials, and finished materials. Results for these tests are reported on analytical reports and certificates of analysis without any evidence or traceability to demonstrate that samples were prepared. Additionally, standards used in the QC laboratory for these tests are identified with a date in the log book titled "Standard Solutions." However, there is no raw data for the preparation of these standards.

c. There is no raw data to support any of the analytical results reported during the re-validation of the water treatment system in 2012.

d. The notebook that documents the raw data obtained during the elemental analysis of materials using the Atomic

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Atul J. Agrawal, Investigator Dipesh Shah, Investigator	April 9, 2013

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	April 1 - 6 & 9, 2013
	FEI NUMBER 3003297374

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Bhailalbhai Nathabhai Patel, Managing Director

FIRM NAME	STREET ADDRESS
Canton Laboratory	110-A & B, GIDC Estate, Makarpura Road
CITY, STATE AND ZIP CODE Vadodara - 390010 India	TYPE OF ESTABLISHMENT INSPECTED API, Excipient & Dietary Supplement Manufacturer

(Document # MVP/01/11) states that manufacturing processes should be validated every (b)(4)

c. The production processes for more than (b)(4) additional materials manufactured as active or inactive ingredients have not been initially validated or re-validated, as required by SOP QAD/017, Validation Approach, and the Validation Master Plan.

OBSERVATION 8

Production operations are not conducted in a manner to prevent contamination of materials being produced.

Specifically, appropriate measures are not present to prevent contamination during the manufacture of active and inactive ingredients. The following deficiencies were observed:

a. The water treatment system (Water Plant), which is used to provide the (b)(4) water used in the manufacture of all active and inactive ingredients, exits into a T junction which has no back flow prevention device. One end of this T junction leads into the Processing Area of Production Plant (b)(4). The other end of this T junction is open. On April 5, 2013, we observed that a chemical company located in an adjacent building used the other end of the T junction at the end of the water treatment system to connect a hose leading into their manufacturing plant.

b. Batches manufactured in the (b)(4) with ID numbers (b)(4)-1 and (b)(4)-2 are not completely covered and protected against contamination. On April 1, 2013, we observed Batch # (b)(4) of (b)(4) being manufactured in these (b)(4). A (b)(4) enclosure attached to these (b)(4) was observed to have a gap of approximately 3 feet.

c. White concrete-like material was observed on a false ceiling directly above the (b)(4); with ID numbers (b)(4)-4 and (b)(4)-5.

d. Two open ports each in (b)(4) 1 and (b)(4)-2, in which (b)(4) are attached, are left open during the (b)(4) process of materials being manufactured. On April 1, 2013, we observed the open ports on these (b)(4). We also observed in-process materials in (b)(4)-1 and (b)(4)-2, which, according to the status tag

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Atul J. Agrawal, Investigator Dipesh Shah, Investigator	April 9, 2013

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	April 1 - 6 & 9, 2013
	FEI NUMBER 3003297374

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Bhailalbhai Nathabhai Patel, Managing Director

FIRM NAME	STREET ADDRESS
Canton Laboratory	110-A & B, GIDC Estate, Makarpura Road
CITY, STATE AND ZIP CODE Vadodara - 390010 India	TYPE OF ESTABLISHMENT INSPECTED API, Excipient & Dietary Supplement Manufacturer

determine whether a problem exists, batches for which OOS results are obtained are released as Analytical Reagent grade material. Our review of the notebook titled "AAS," in which data for elemental analysis is minimally entered, found at least 8 entries that employees underlined (no batch numbers noted). The QC Manager stated that in each of these instances, the batch did not meet the specification for the test and was released as Analytical Reagent grade material. The OOS result was not documented or investigated.

c. We found two sets of reported data for the following materials:

i. The (b)(4) Water sample with A.R. # MB/(b)(4) /03; there are two Microbial Limit Test Reports for this sample, each with the same test date (2/2/2013) and QA Issue number (#37). A review of these reports found different individual results and overall limits reported for the same A.R. Number.

ii. The Source Water sample with A.R. # MB/SO/03; there are two Microbial Limit Test Reports for this sample, each with the same test date (2/2/2013) and QA Issue number (#36). A review of these reports found different individual results reported for the same A.R. Number.

OBSERVATION 10

Routine calibration of equipment critical for ensuring the quality of materials being manufactured is not performed.

Specifically, the (b)(4) in the (b)(4)) with ID numbers (b)(4) -1 and (b)(4) -2 are not calibrated. These (b)(4) are used to (b)(4) , which are critical parameters during the (b)(4) step of active and inactive ingredients being manufactured. There is no documentation or evidence to demonstrate that these (b)(4) have ever been calibrated or checked. Both (b)(4) were last qualified in 2009.

OBSERVATION 11

Non-dedicated equipment used in manufacturing is not adequately cleaned.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Atul J. Agrawal, Investigator Dipesh Shah, Investigator	April 9, 2013

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	April 1 - 6 & 9, 2013
	FEI NUMBER 3003297374

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Bhailalbhai Nathabhai Patel, Managing Director

FIRM NAME	STREET ADDRESS
Canton Laboratory	110-A & B, GIDC Estate, Makarpura Road
CITY, STATE AND ZIP CODE Vadodara - 390010 India	TYPE OF ESTABLISHMENT INSPECTED API, Excipient & Dietary Supplement Manufacturer

Specifically,

a. The stability characteristics of the API (b)(4) USP are not monitored. No stability studies (accelerated or long-term) have been conducted for this API and no batches are being monitored for stability. A (b)(4) retest date is assigned for (b)(4) USP and is not based on any evaluation of data derived from stability studies.

b (b)(4) commercial batch per (b)(4) of each pharmaceutical grade product is not placed on stability, as required by SOP # QCD/022, Stability Studies of Pharmaceutical Products. For example, no a commercial batch of (b)(4) (b)(4) manufactured in 2012 is not on stability.

c. SOP # QCD/022 states that accelerated stability studies shall be conducted at (b)(4), and (b)(4) months. However, we found that accelerated stability studies for (b)(4) USP batches (b)(4), and (b)(4) manufactured in 2011 were conducted for (b)(4), and (b)(4) months only. Stability analyses were not performed at the (b)(4) and (b)(4) months intervals.

d. The expiry dates on all pharmaceutical active and inactive materials have been changed to retest dates without an evaluation of data derived from stability studies.

OBSERVATION 15

Compendial methods are not verified under actual conditions of use.

Specifically, verifications for compendial tests related to more than (b)(4) items manufactured as pharmaceutical grade materials (active and inactive) have never been conducted. The compendial tests for the raw materials used to manufacture these materials have also not been conducted.

OBSERVATION 16

The system for managing quality does not encompass the resources necessary to ensure confidence that procedures

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	April 1 - 6 & 9, 2013 FEI NUMBER 3003297374

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Bhailalbhai Nathabhai Patel, Managing Director

FIRM NAME	STREET ADDRESS
Canton Laboratory	110-A & B, GIDC Estate, Makarpura Road
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Vadodara - 390010 India	API, Excipient & Dietary Supplement Manufacturer

and processes are effectively implemented and all manufactured materials meet intended specifications for quality and purity.

Specifically, an effective system for managing quality has not been implemented. Currently, all quality-related activities are overseen by (b) (4) individual. The deficiencies identified in this inspection indicate that management has not allocated the necessary resources to ensure that all necessary quality-related activities are completed. Examples of deficiencies identified and cited during this inspection include, but are not limited to:

a. The validation and qualification requirements for production processes and equipment, respectively, are not met;
b. Product Quality Reviews for all manufactured materials are not conducted, as required by SOP # QAD/028, Product Quality Review;
c. Investigations are not thoroughly conducted;
d. Deviations during production are not documented and evaluated to determine if they are critical; and
e. Batches are released without a thorough evaluation of whether specifications are met (e.g., Batches (b) (4) (b) (4) and (b) (4) of (b) (4) USP were released for distribution without the requisite microbiological analyses).

OBSERVATION 17

Entries in records are deficient.

Specifically, we found the following deficiencies in records we reviewed:

a. We observed numerous corrections to entries that were not dated and signed or made in a manner to leave the original entry still legible. These observations were pointed out to the QA, QC, and Production Manager throughout the inspection. Except for one instance, we found that these numerous corrections were made by overwriting over the original entry. In this manner, the original and corrected entries are not legible. Examples of the types of entries for which we found corrections include, but are not limited to:
i. Batch numbers;
ii. Raw and analytical data;
iii. Dates in batch production records;

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (*Print or Type*)	DATE ISSUED
		Atul J. Agrawal, Investigator Dipesh Shah, Investigator	April 9, 2013

BAXTER Pharma 483 – posted this week – from Obs 1 – 4. (multiple OOS for US marketed product)

URL: Compliance Document Baxter Pharm. India (fda.gov)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	1/19/2023-1/27/2023*
	FEI NUMBER 3004610460

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Rishikesh Jaiwant, Senior Director Manufacturing & Operations

FIRM NAME	STREET ADDRESS
Baxter Pharmaceuticals India Pvt Ltd	Village Vasana Chacharwadi, Taluka Sanand
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Ahmedabad, Gujarat, 382213 India	Drug Manufacturer

Date OOS Investigation Logged: 10-Jan-2022
Date OOS Investigation Closed: 23-Feb-2022
Root cause: (b) (4) functioning of the HPLC

On January 10, 2022, your QC laboratory obtained failing result for individual unknown impurity at RT (b) (4) which you confirmed through hypothesis test on the original HPLC ID: EQP/QC/418 and ruled-out any issue with HPLC instrument, analyst and retention times, theoretical plates and tailing factor. Your QC laboratory changed HPLC systems without any scientific justification to "repeat" the analysis using freshly prepared mobile phase, standard and sample test solutions. Your firm attempted to complete "repeat" analysis on different HPLC systems for multiples days, however the repeat analysis was aborted at the system suitability stage due to incidents as mentioned below:

-HPLC ID: EQP/QC/304, Dated analysis initiated: 25-Jan-2022, Incident: (b) (4) peak not eluted/missing in standard
-HPLC ID: EQP/QC/308, Dated analysis initiated: 31-Jan-2022, Incident: Improper peak shape of (b) (4) peak

In the above two (2) cases, your firm deviated from SOP Document No.: CF/QCD/002, Revision: C, Titled: "*Handling of Laboratory Incidences*". Your firm did not log the incident to investigate the issues pertaining to missing (b) (4) peak and for improper peak shape of (b) (4) peak.

The overall assessment of OOS logged for the US market in years 2021 and 2022 revealed three (3) out of fifty-two (52) OOS having laboratory incidents during OOS investigation. However, your firm did not log a separate LIR to investigate the root cause. Furthermore, in the same period of years 2021 and 2022, your firm changed the HPLC instrument in seven (7) OOS investigations without any scientific justification and invalidated the original failing results

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Justin A Boyd, Investigator Pratik S Upadhyay, Investigator - Dedicated Drug Cadre X	1/27/2023

Kilitch 483 – Obs 2 – DI – do not collect samples

URL: Compliance Document: Kilitch Healthcare India Limited (fda.gov)

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Paresh Mehta, Managing Director	
FIRM NAME: Kilitch Healthcare India Limited	STREET ADDRESS: R - 904 905 T T C Industrial Road
CITY, STATE, ZIP CODE, COUNTRY: Navi Mumbai, Maharashtra, 400706 India	TYPE ESTABLISHMENT INSPECTED: Sterile Drug Manufacturing Facility

OBSERVATION 2

Laboratory records do not include complete data derived from all tests, examinations and assay necessary to assure compliance with established specifications and standards.

1. Microbiologists responsible for collecting environmental monitoring and personnel monitoring samples confirmed they do not collect all samples due to workload. Microbiologists also explained personnel monitoring samples may not be collected due to production personnel that refuse to submit to personnel monitoring. For samples that are not collected, a result is still recorded in the reported laboratory records that is below the alert limit and within trend of previous data. The practice of not collecting all samples, but still reporting conforming results has been occurring for at least one year.

    a. Inspection of the incubators in the microbiology laboratory on October 12, 2023, identified environmental monitoring and personnel monitoring samples that were supposed to have been collected during aseptic manufacturing on (b) (4) Lines (b) (4) and (b) (4) were not present. Logbooks with testing dates and incubator use logs documented samples, which were not present. Examples of missing samples included:

        i. Personnel monitoring samples including (b) (4) plates from (b) (4) body locations and (b) (4) finger dab plates for each person that had worked in the aseptic fill room for each day. From October 6-11, 2023, the aseptic entry and exit log documented there should have been approximately 102 sets of plates, containing (b) (4) plates for each person, under incubation. Only 3 sets of plates were present in the incubator.

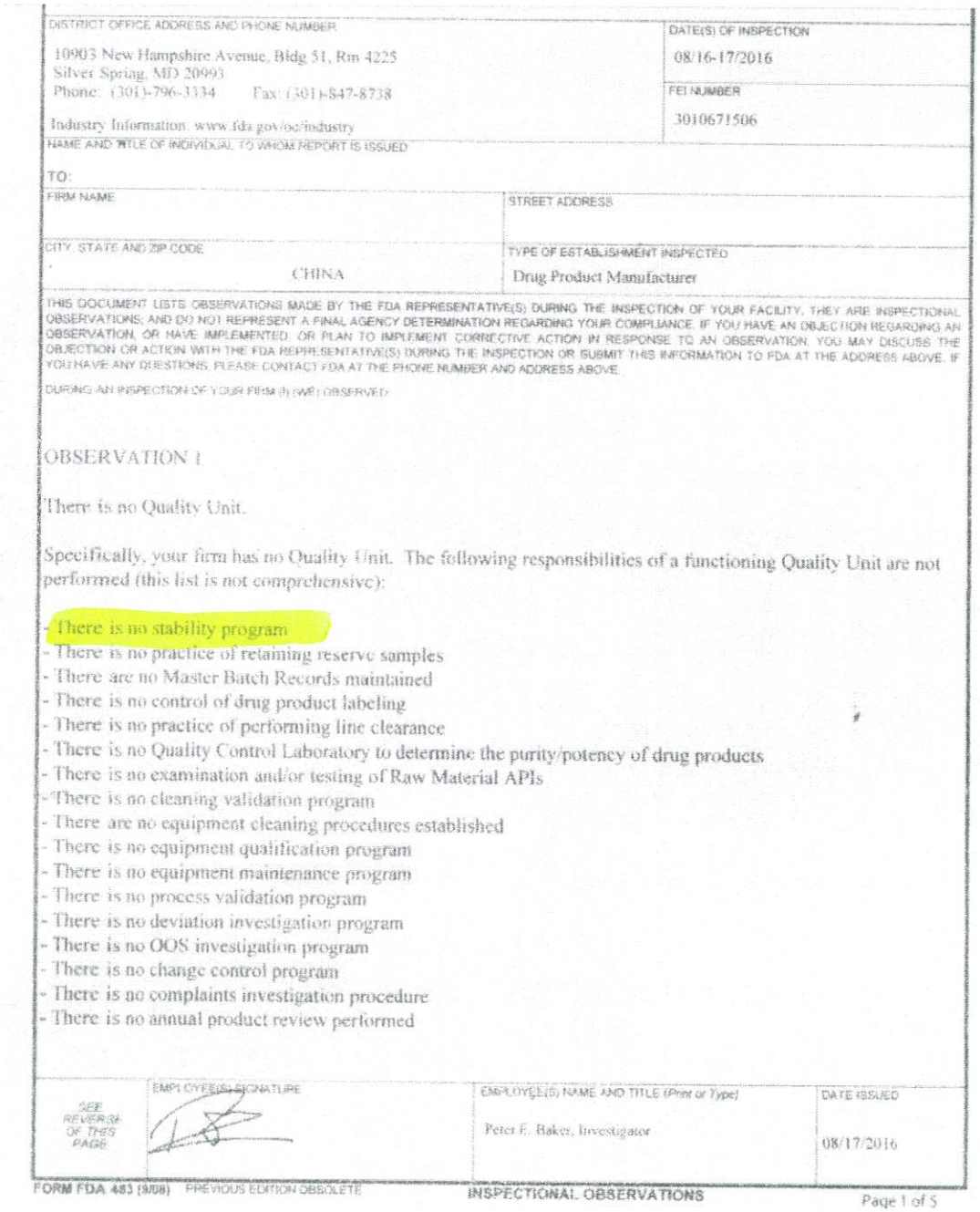
        ii. All post filling swab sample of surfaces inside the filling (b) (4) associated with (b) (4) batches (b) (4).

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE: Anastasia M Shields, Investigator Justin A Boyd, Investigator	X	DATE ISSUED: 10/20/2023

FORM FDA 483 (09/08) PREVIOUS EDITION OBSOLETE INSPECTIONAL OBSERVATIONS PAGE 3 of 19 PAGES

This is a Peter Baker classic, that I posted back in AUGUST 2017
URL: Zhejiang Bangli Medical Products Co., Yongkang City, China 8.17.16 483 (fda.gov)

"YES, We Have No Quality [Unit]" - this 483 from AUG2016 must have been an interesting one for the redoubtable Peter Baker to prepare. It covers 5 pages but Obs #1 on Page 1 sums it up well in one sentence - "There is no quality Unit." While that would be brief but accurate, the text goes on, Click the graphic to see the full first page. [Full text w/o my redactions may be found at www.fda.gov, refer: ucm566017]
Direct link [updated 20MAY2020]: https://lnkd.in/ePR4kXQ



DISTRICT OFFICE ADDRESS AND PHONE NUMBER
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

DATE(S) OF INSPECTION
08/16-17/2016

FEI NUMBER
3010671506

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED
TO:

FIRM NAME

STREET ADDRESS

CITY, STATE AND ZIP CODE
CHINA

TYPE OF ESTABLISHMENT INSPECTED
Drug Product 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

There is no Quality Unit.

Specifically, your firm has no Quality Unit. The following responsibilities of a functioning Quality Unit are not performed (this list is not comprehensive):

- There is no stability program
- There is no practice of retaining reserve samples
- There are no Master Batch Records maintained
- There is no control of drug product labeling
- There is no practice of performing line clearance
- There is no Quality Control Laboratory to determine the purity/potency of drug products
- There is no examination and/or testing of Raw Material APIs
- There is no cleaning validation program
- There are no equipment cleaning procedures established
- There is no equipment qualification program
- There is no equipment maintenance program
- There is no process validation program
- There is no deviation investigation program
- There is no OOS investigation program
- There is no change control program
- There is no complaints investigation procedure
- There is no annual product review performed

SEE REVERSE OF THIS PAGE

EMPLOYEE(S) SIGNATURE

EMPLOYEE(S) NAME AND TITLE (Print or Type)
Peter E. Baker, Investigator

DATE ISSUED
08/17/2016

FORM FDA 483 (9/08) PREVIOUS EDITION OBSOLETE INSPECTIONAL OBSERVATIONS Page 1 of 5

EOD – apologies that I could not find 'the wheelbarrow" reference .... ***JTE 02 FEB 2024***

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10903 New Hampshire Ave,Bldg 51,Rm 4225 Silver Springs, MD 20993 (301) 796-3334 Fax:(301) 847-8738 Industry Information: www.fda.gov/oc/industry	03/18/2014 - 03/22/2014* FEI NUMBER 3008316085

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
TO: Zena Kaufman, Senior Vice President - Global Quality

FIRM NAME	STREET ADDRESS
Hospira Healthcare India Pvt Ltd	Plot No. 117 Jawaharlal Nehru Pharma City SEZ
CITY, STATE, ZIP CODE, COUNTRY Parawada Mandal, Visakhapatnam 531 019, India	TYPE ESTABLISHMENT INSPECTED Finished Drug Product Manufacturer

Notably, during my examination of your firm's visual inspection operator qualification kit for [redacted] bottles, I found that there are no representative examples for the minor defect "dent" category included.

OBSERVATION 8

There is a lack of written procedures describing in sufficient detail the methods, equipment and materials to be used for sanitation.

Specifically, during my inspection of the [redacted] (b)(4) manufacturing block on 03/18/14, I found that there are no written procedures available in a language understandable by the majority of contract personnel, who are primarily engaged in the cleaning and sanitation of auxiliary areas.

OBSERVATION 9

Production personnel were not practicing good sanitation and health habits.

Specifically, during my inspection of the washing and toilet facility located at the entrance to the [redacted] (b)(4) manufacturing unit on 03/21/14, I observed three out of [redacted] (b)(4) employees from the QC and Manufacturing departments use and leave the facility without washing their hands with soap.

OBSERVATION 10

Buildings used in the manufacture, processing, packing or holding of drug products are not free of infestation by rodents, birds insects, and other vermin.

Specifically, during my inspection of the washing and toilet facility located at the entrance to the [redacted] (b)(4) manufacturing unit on 03/21/14, I observed what appeared to be a mosquito within the facility. My subsequent examination of the "shaft room" located as an access corridor between the washing/toilet facility and the gowning/change room found a significant pooling of water and TNTC insects. A broken screen was observed, which appeared to allow the entrance of pests into the washing/toilet facility.

* DATES OF INSPECTION:
03/18/2014(Tue), 03/19/2014(Wed), 03/20/2014(Thu), 03/21/2014(Fri), 03/22/2014(Sat)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Peter E. Baker, Investigator PB	03/22/2014