IMPAX LABORATORIES INC

FORM 8-K
(Current report filing)

Filed 03/04/13 for the Period Ending 03/04/13

Address	30831 HUNTWOOD AVENUE HAYWARD, CA 94544
Telephone	510-240-6000
CIK	0001003642
Symbol	IPXL
SIC Code	2834 - Pharmaceutical Preparations
Industry	Biotechnology & Drugs
Sector	Healthcare
Fiscal Year	12/31

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the
Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): March 4, 2013

Impax Laboratories, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-34263**	**65-0403311**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

30831 Huntwood Avenue, Hayward, CA	**94544**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **(510) 240-6000**

Not Applicable

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 7.01 Regulation FD Disclosure.

On March 4, 2013, Impax Laboratories, Inc. (the "Company") issued a press release announcing its receipt of a Form 483 from the U.S. Food and Drug Administration (the "FDA") related to the FDA's inspection of the Company's Hayward, California manufacturing facility. A copy of the press release is attached hereto as Exhibit 99.1 and a redacted copy of the Form 483 issued by the FDA is attached hereto as Exhibit 99.2, each of which is incorporated by reference herein.

This Current Report on Form 8-K and the information in this Item 7.01 hereof, including the exhibits attached hereto, will not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), nor will it be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act unless expressly identified therein as being specifically incorporated therein by reference.

"Safe Harbor" statement under the Private Securities Litigation Reform Act of 1995:

To the extent any statements made in this Current Report on Form 8-K contain information that is not historical, these statements are forward-looking in nature and express the beliefs and expectations of management. Such statements are based on current expectations and involve a number of known and unknown risks and uncertainties that could cause actual developments and results to differ significantly from those that are expressed or implied by such forward-looking statements. Such risks and uncertainties include, but are not limited to, the effect of current economic conditions on the Company's industry, business, financial position and results of operations, fluctuations in revenues and operating income, the Company's ability to promptly correct the issues raised in the warning letter received from the FDA, the Company's ability to successfully develop and commercialize pharmaceutical products in a timely manner, reductions or loss of business with any significant customer, the impact of consolidation of the Company's customer base, the impact of competition, the Company's ability to sustain profitability and positive cash flows, any delays or unanticipated expenses in connection with the operation of the Company's Taiwan facility, the impact of market perceptions of the Company and the safety and quality of the Company's products, the difficulty of predicting FDA filings and approvals, the Company's ability to comply with legal and regulatory requirements governing the healthcare industry, the regulatory environment and other risks described in the Company's periodic reports filed with the Securities and Exchange Commission . Forward-looking statements speak only as to the date on which they are made, and the Company undertakes no obligation to update publicly or revise any forward-looking statement, regardless of whether new information becomes available, future developments occur or otherwise, except to the extent required by applicable law.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.
The following exhibits are furnished herewith.

Exhibit No.	Description
99.1	Press release issued March 4, 2013
99.2	FDA Form 483

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: March 4, 2013

IMPAX LABORATORIES, INC .

By: /s/ Bryan M. Reasons

Name: Bryan M. Reasons

Title: Senior Vice President, Finance, and Chief Financial Officer

EXHIBIT INDEX

Exhibit No.	Description
99.1	Press release issued March 4, 2013
99.2	FDA Form 483

Exhibit 99.1

Company Contact:
Impax Laboratories, Inc.
Mark Donohue
Sr. Director, Investor Relations and Corporate Communications
(215) 558-4526
www.impaxlabs.com

Impax Provides an Update on FDA Inspection of Hayward Facility

Conference Call and Webcast Scheduled for 5:00 p.m. ET

HAYWARD, Calif., March 4, 2013 – Impax Laboratories, Inc. (NASDAQ: IPXL) today announced that the U.S. Food and Drug Administration (FDA) completed its re-inspection of the Company's Hayward manufacturing facility in connection with the previously disclosed Form 483 issued in March 2012. In addition to the re-inspection, the FDA conducted a Pre-Approval Inspection (PAI) for RYTARY ™, as analytical method validation and a portion of the stability data were generated in Hayward, and a general Good Manufacturing Practices (GMP) inspection. At the conclusion of this inspection, the FDA issued a new Form 483 with twelve (12) observations, three (3) of which are designated as repeat observations from inspections that occurred prior to the Warning Letter.

"We have committed significant resources in our efforts to meet FDA requirements and are clearly disappointed by this news," said Larry Hsu, Ph.D., president and CEO, Impax Laboratories, Inc. "The analytical method assessment observations arose from our internal work and review as a part of the ongoing quality improvement program designed to assess and enhance our Quality Control Laboratory Analytical Methods and to ensure they meet or exceed internal and industry standards. Resolving the FDA concerns remains a top priority and we intend to complete this work as quickly as possible."

The Company is working diligently to address the observations raised by the FDA and will respond to these new observations within the fifteen (15) business day period from the receipt of the Form 483.

Currently, the Company has not been informed by the FDA of the impact this latest Form 483 will have on the resolution or timing of resolving the warning letter or whether any further regulatory action may be taken as to its manufacturing operations. Until remedial action is complete and the FDA has confirmed compliance with current GMP, approval of pending and new applications listing the Hayward facility as a manufacturing location of finished dosage forms may be withheld.

The Company has provided a redacted version of the Form 483 as an exhibit in a Current Report on Form 8-K filed with the SEC concurrently with the issuance of this press release.

Conference Call Information
The Company will host a conference call today at 5:00 p.m. EDT. The call can also be accessed via a live Webcast through the Investor Relations section of the Company's Web site, www.impaxlabs.com . The number to call from within the United States is (877) 356-3814 and (706) 758-0033 internationally. The conference ID is 18793480. A replay of the conference call will be available shortly after the call for a period of seven days. To access the replay, dial (855) 859-2056 (in the U.S.) and (404) 537-3406 (international callers).

About Impax Laboratories, Inc.
Impax Laboratories, Inc. (Impax) is a technology based specialty pharmaceutical company applying its formulation expertise and drug delivery technology to the development of controlled-release and specialty generics in addition to the development of central nervous system disorder branded products. Impax markets its generic products through its Global Pharmaceuticals division and markets its branded products through the Impax Pharmaceuticals division. Additionally, where strategically appropriate, Impax develops marketing partnerships to fully leverage its technology platform and pursues partnership opportunities that offer alternative dosage form technologies, such as injectables, nasal sprays, inhalers, patches, creams and ointments. Impax Laboratories is headquartered in Hayward, California, and has a full range of capabilities in its Hayward, Philadelphia and Taiwan facilities. For more information, please visit the Company's Web site at: www.impaxlabs.com .

"Safe Harbor" statement under the Private Securities Litigation Reform Act of 1995:

To the extent any statements made in this news release contain information that is not historical, these statements are forward-looking in nature and express the beliefs and expectations of management. Such statements are based on current expectations and involve a number of known and unknown risks and uncertainties that could cause the Company's future results, performance or achievements to differ significantly from the results, performance or achievements expressed or implied by such forward-looking statements. Such risks and uncertainties include, but are not limited to, the effect of current economic conditions on the Company's industry, business, financial position and results of operations, fluctuations in revenues and operating income, the Company's ability to promptly correct the issues raised in the warning letter received from the FDA, the Company's ability to successfully develop and commercialize pharmaceutical products in a timely manner, reductions or loss of business with any significant customer, the impact of consolidation of the Company's customer base, the impact of competition, the Company's ability to sustain profitability and positive cash flows, any delays or unanticipated expenses in connection with the operation of the Company's Taiwan facility, the effect of foreign economic, political, legal and other risks on the Company's operations abroad, the uncertainty of patent litigation, the increased government scrutiny on the Company's agreements with brand pharmaceutical companies, consumer acceptance and demand for new pharmaceutical products, the impact of market perceptions of the Company and the safety and quality of the Company's products, the difficulty of predicting FDA filings and approvals, the Company's ability to achieve returns on its investments in research and development activities, the Company's inexperience in conducting clinical trials and submitting new drug applications, the Company's ability to successfully conduct clinical trials, the Company's reliance on third parties to conduct clinical trials and testing, impact of illegal distribution and sale by third parties of counterfeits or stolen products, the availability of raw materials and impact of interruptions in the Company's supply chain, the use of controlled substances in the Company's products, disruptions or failures in the Company's information technology systems and network infrastructure, the Company's reliance on alliance and collaboration agreements, the Company's dependence on certain employees, the Company's ability to comply with legal and regulatory requirements governing the healthcare industry, the regulatory environment, the Company's ability to protect its intellectual property, exposure to product liability claims, changes in tax regulations, the Company's ability to manage growth, including through potential acquisitions, the restrictions imposed by the Company's credit facility, uncertainties involved in the preparation of the Company's financial statements, the Company's ability to maintain an effective system of internal control over financial reporting, the effect of terrorist attacks on the Company's business, the location of the Company's manufacturing and research and development facilities near earthquake fault lines and other risks described in the Company's periodic reports filed with the Securities and Exchange Commission. Forward-looking statements speak only as to the date on which they are made, and the Company undertakes no obligation to update publicly or revise any forward-looking statement, regardless of whether new information becomes available, future developments occur or otherwise.

# # #

Exhibit 99.2

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
1431 Harbor Bay Parkway Alameda, CA 94502-7070 (510) 337-6700 Fax:(510) 337-6702 Industry Information: www.fda.gov/oc/industry	01/08/2013 - 02/28/2013* FEI NUMBER 3004182921

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Chungchiang Hsu, President & Chief Executive Officer

FIRM NAME	STREET ADDRESS
Impax Laboratories, Inc.	31145 San Antonio Street
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Hayward, CA 94544-7905	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:

OBSERVATION 1

The accuracy, sensitivity, specificity, and reproducibility of test methods have not been established.

Specifically,

Pertaining to NDA 203312 Levodopa/Carbidopa IPX066

A. The method validation performed for NDA 203312: Rytary (IPX066) (Levodopa/Carbidopa Capsule) finished drug products as specified in [redacted] is inadequate. For example:

1) The firm failed to establish specifications (evaluate, identify, monitor, and test) for the [redacted] and/or [redacted] that are identified on the COA for API, levodopa, manufactured by [redacted].

2) The impurity profile does not include these [redacted] impurities in the finished stability product.

3) The specificity of the test method is not established because the [redacted] studies were not performed under [redacted] conditions.

4) The [redacted] used for lot release and retesting of the carbidopa and levodopa API is not [redacted]

5) Water determination using [redacted] for components [redacted] was not validated.

6) The firm is not testing for the [redacted] in the levodopa API during release.

7) The study to determine the [redacted] was inadequate. The firm's [redacted] was not determined with a fully validated method because it lacked accuracy and linearity to cover the validation ranges. [redacted] was based on [redacted] of Levodopa. [redacted] utilizing placebo samples (free of the active) was not studied and no comparison of [redacted] to a [redacted] standard.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Daniel J. Roberts, Investigator DJR Walden H. Lee, Chemist Kim L. Thomas Cruse, Chemist Kim Thomas Cruse	02/28/2013

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Hayward, CA 94544-7905

TYPE ESTABLISHMENT INSPECTED
Drug Manufacturer

Commercial Products

B. Non-suitable test methods are used to release finished drug products.

1) During the establishment inspection, we reviewed test methods for eighteen (18) products and found that 100% of the reviewed methods were not properly validated. For example, accuracy, sensitivity, linearity, LOD, LOQ, and/or specificity were not assessed in the method validations. There is no assurance of the reliability of the data and results generated with the use of the following test methods:

Inadequate Test Methods/Non-Validated Test Methods

Product	Loss on Drying	Chromatographic Purity/Related Substances	Dissolution	Content Uniformity	Assay
Acarbose Tablets	NV	IV	IV	IV	IV
Bethanechol Cl Tablets		IV	IV	IV	IV
Bupropion HCl/ ER (XL) Tablets	NV	IV	IV	IV	IV
Carbidopa/ Levodopa ER Tablets	NV	IV	IV	IV	IV
Fenofibrate Tablets		IV	IV	IV	IV
Nadolol/ Bendroflumethiazide Tablets	NV	IV	IV	IV	IV
Colestipol Tablets		IV		IV	IV
Carprofen Tablets	NV	IV	IV	IV	IV
Tamsulosin Hydrochloride Capsules		IV		IV	IV
Pyridostigmine Bromide Tablets		IV	IV	IV	IV
Terbutaline Sulfate Tablets	NV				

SEE REVERSE OF THIS PAGE

EMPLOYEE(S) SIGNATURE
Daniel J. Roberts, Investigator
Walden H. Lee, Chemist
Kim L. Thomas Cruse, Chemist

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Hayward, CA 94544-7905

TYPE ESTABLISHMENT INSPECTED
Drug Manufacturer

Inadequate Test Methods/Non-Validated Test Methods

Product	Loss on Drying	Chromatographic Purity/Related Substances	Dissolution	Content Uniformity	Assay
Chloroquin Phosphate Tablets	NV				
Dipyridamole Tablets	NV				
Loratadine Tablets	NV				
Primidone Tablets	NV				
Orphenadrine Citrate Tablets	NV				
Oxybutynin HCl Tablets	NV				
Oxymorphone HCl Tablets	NV				

NV= No Validation Data IV= Inadequate Validation Data

2) [redacted] The analytical methods include, but are not limited to, identification; assay; content uniformity; dissolution and related substance. As of 2/8/2013, QC and/or QA approved and concurred with [redacted] of these assessments. The firm continues to analyze and release products with these methods regardless of the known deficiencies.

Lots Released with Deficient Test Methods

Product	Dosage	Lot #
Acarbose Tablets	25, 50, 100 mg	H0030371, 10000593, 10004381,10002860, 10002859, 10004380, 10000595, 10001534, H9071531
Bethanechol Cl Tablets	5,10, 25, 50 mg	H0091541, 10003129, 10001683, 10001801

SEE REVERSE OF THIS PAGE

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Lots Released with Deficient Test Methods		
Product	**Dosage**	**Lot #**
Bupropion HCl ER Tablet	100, 150, 200 mg	10000516, 10005195, 10003829
Carbidopa/Levodopa ER Tablets	25/100, 50/200 mg	10000700, 10000803, 10000804, H9101291, H9101551, H9101341, H9101351
Fenofibrate Capsules	54, 160 mg	10001036, 10001037, 10001294, 10001223, 10001293, 10002865
Nadolol/Bendroflumethiazide Tablet	40/5, 80/5 mg	10005261, 10003033, 10001642

3) The firm failed to determine the acceptability of test methods prior to using them in the QC laboratory through formal method transfer procedures. The test methods are currently used by the QC laboratory to release raw and in-process materials, finished drug products, and stability samples. SOP 2ALY-012.07, "Transfer of Analytical Test Method", effective on 8/15/12, states in Section 2.2: *This procedure applies to the transfer of validated, non-compendial, analytical test methods from the Originating Laboratory (OL) to the Receiving Laboratory (RL) (including transfers to and from an Impax laboratory to a contract laboratory).* Examples includes:

Inadequate Method Transfer	
Product	**Test Method**
Loratadine/Pseudoephedrine ER Tablets	Assay, Dissolution, Related Substances
Sotalol HCl Tablets	Assay, Content Uniformity, Dissolution, Related Substances
Terbutaline Sulfate Tablets	Assay, Content Uniformity, Dissolution, Related Substances

4) Impax uses test methods that are not stability indicating to re-test and release active pharmaceutical ingredients (API) used in the production of finished drug products. Examples include:

a. The firm uses USP assay test method (Titration Method) for Pyridostigmine Bromide API, for raw material retest. Titration is not a stability indicating method and cannot detect unknown degradants. For example, Pyridostigmine Bromide purchased from the API manufacturer [redacted] lot 0000124010 with retest dates (re-evaluation) of November 24, 2009, were retested by the firm using the USP titration method. This API lots were used in the manufacture of Pyridostigmine Bromide 60 mg tablets lots H004130 approved June 23, 2010.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Daniel J. Roberts, Investigator Walden H. Lee, Chemist Kim L. Thomas Cruse, Chemist	DATE ISSUED 02/28/2013

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b. The firm uses USP assay test method for Bendroflumethiazide API (a titration method) for raw material retest. Titration method is not a stability indicating method and cannot detect unknown degradants. For example, Bendroflumethiazide purchased from the API manufacturer [redacted] lot RBNZP10027 with retest date (re-evaluation) of September 4, 2012, and was retested by the firm using the USP titration method. This API lot was used in the manufacture of Nadolol/Bendroflumethiazide 40/5 mg tablets lot 10005844 approved November 30, 2012.

c. The firm uses USP assay test method for Pseudoephedrine Sulfate API (a titration method) for raw material retest. Titration is not a stability indicating method and cannot detect unknown degradants. For example, Pseudoephedrine Sulfate purchased from the API vendor [redacted] lot 232382AX10 with retest date (re-evaluation) of September 1, 2009, was retested by the firm using the USP titration method. This API lot was used in the manufacture of Loratadine/Pseudoephedrine Sulfate 5/120 mg tablets lot H909131 approved November 18, 2009.

REPEAT OBSERVATION

OBSERVATION 2

Control procedures are not established which validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug product.

Specifically,

Pertaining to NDA 203312 Levodopa/Carbidopa IPX066

A. The firm's [redacted] There is no assurance that the results generated from these studies are accurate and precise.

Furthermore, the [redacted] hold time data submitted for intermediate components [redacted] and [redacted] finished bulk drug product was not complete at the time of filing this application.

B. [redacted] deviations occurred during the execution of the [redacted] studies for the finished bulk drug product. These deviations included the following:

1. [redacted]
2. [redacted]

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These deviations were never discussed or evaluated in the [redacted] validation report.

Commercial Products

Established manufacturing process parameters are not always validated.

C. The established sampling plans during process validations are not statistically representative of the batch size. For example, the firm uses the generic sampling plan to collect [redacted] samples from the blender for blend uniformity and [redacted] samples for dissolution during compression/encapsulation irrespective of the batch size of [redacted] units or [redacted] million units.

D. The inlet air temperature used during coating to accelerate the drying process of hygroscopic Colestipol tablets has an established process parameter of [redacted] °C and a target of [redacted] °C in the batch production record. The validation data only supports a process parameter range of [redacted] °C.

1. In 2012, 33 of the 51 Colestipol 1000 mg tablets batches manufactured were outside the validated process parameter range of [redacted] °C during the coating process. The firm has received [redacted] complaints of swollen Colestipol tablets in 2012.

E. The compression force feeder speed that is used to maintain uniform die fill and compressibility during tablet compression for Carprofen tablets has an established process parameter of [redacted] RPM in the batch production record. The validation data only supports a process parameter of [redacted] RPM.

F. On 1/8/2013 during a tour of [redacted] warehouse, we observed several in-process materials being stored at the compounding, blending, and compression stage of the manufacturing process. SOP #2QUA-036.06: Tracking Bulk Holding Date of Intermediate and Finished Product in SAP states that in-process hold-times in the warehouse are established at [redacted] days. The firm has no scientific data through validation to support the assigned [redacted] days.

REPEAT OBSERVATION

OBSERVATION 3

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,
There is a failure to thoroughly review and document unexplained discrepancies. Examples include:

A. The cleaning solution rinse water from the Sampling Thief-3ft [redacted] was tested on 07/25/2012 and unknown peaks were identified on the HPLC chromatogram. There is no deviation report, investigation, or root cause assessment for the unidentified peak observed in the HPLC chromatogram from this test. The sample was re-injected twice and re-vialed without documentation.

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B. [redacted] complaints from [redacted] different lots were received for broken tablets of Carprofen 75mg and Carprofen 100mg between September and November 2012. During the investigation of these complaints, broken tablets were confirmed in [redacted] of the [redacted] complaint lots. In addition, [redacted] broken tablets were also observed in the Carprofen 100mg lot H0010072 during 104 week stability sample testing. The investigations failed to identify the root cause and stated that broken Carprofen tablets are a known occurrence.

C. Deviation PR ID #: 1302 was initiated to investigate condensation and clumping in [redacted] drums of RM-5344: Pyridostigmine Bromide, USP, lot 0000001913. This API is hygroscopic, thus sensitive to temperature / humidity. The deficiencies in this investigation report are as follows:

1. It fails to address the impact of the warehouse storage conditions especially since the firm does not monitor humidity in the warehouse.

2. This deviation report fails to explain why assay for Pyridostigmine Bromide, USP, lot 0000001913 was not performed prior to use to manufacture finished drug product: Pyridostigmine Bromide 60 mg tablets lots 10003307 and 10003308.

OBSERVATION 4

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,

Pertaining to NDA 203312 Levodopa/Carbidopa IPX066

A. The software that controls the [redacted] used for NDA 203312 Rytary (IPX066) were not validated. These instruments/equipment were used to analyze the NDA product. The firm did not validate the instruments data integrity acquisition system to ensure that analysts cannot re-write or delete analytical data during analyses. Data audit trails are not maintained and instrument audit logs are not saved. These instruments generated data for the NDA submission.

Commercial Products

B. [redacted] moisture analyzer and UV spectrophotometer are used for raw material and finished product release testing. The firm did not validate the instruments data integrity acquisition system to ensure that analysts cannot re-write or delete analytical data during analyses. Data audit trails are not maintained and instrument audit logs are not saved. These instruments are used in the quality control and research and development laboratories.

C. The in-process weight checks performed during the compression and encapsulation process are performed on equipment scales that allow all production personnel to alter dates and time when performing these in-process weight checks. In addition, the hardness test machine, [redacted] allows for printing of tablet

hardness raw data results during in-process testing. However, the firm has never enabled this function, hence does not have or store raw data of this operation during production or process validations.

OBSERVATION 5

Written procedures for cleaning and maintenance fail to include description in sufficient detail of methods, equipment and materials used, description in sufficient detail of the methods of disassembling and reassembling equipment as necessary to assure proper cleaning and maintenance, and parameters relevant to the operation.

Specifically,

Cleaning procedures and operations are deficient. Examples include:

A. The cleaning validation protocol failed to address the swab location and the swabbing technique on manufacturing equipment during cleaning validation.

B. Swab studies have not been performed to determine the best swab for maximum recovery of active ingredient and other chemical residues after the cleaning operation of non-dedicated manufacturing equipment.

C. There's a failure to establish scientific rationale for the use of 99% Isopropyl Alcohol as a cleaning agent on production equipment used to manufacture finished drug products.

D. During the cleaning validation of Terbutaline Sulfate, two (2) lots (lot# 20804, lot# 20904) failed maximum Terbutaline Sulfate chemical product carryover after the initial cleaning process from the [redacted] spray gun. The equipment was re-cleaned and the incident was never discussed in the cleaning validation summary report.

E. Equipment swab locations performed during the monthly routine cleaning monitoring do not always include the most difficult to clean equipment parts specified in SOP 2VAL-001: Cleaning Verification and Validation Program.

   1) For example, not all difficult to clean equipment parts included in this procedure are tested during monthly routine cleaning monitoring. The Valve Seat and Outlet Grate parts specified for routine sampling on the [redacted] are not performed. Additionally, SOP 2VAL-001: Cleaning Verification and Validation Program does not include the cleaning verification of non-dedicated sampling thief used for sampling multiple raw materials and APIs.

F. On 1/11/2013, during a tour of production area in [redacted] we observed the storage of loose rayon ball swabs used for swabbing cleaned manufacturing equipment for the evaluation of API and chemical residue in a glass beaker. These rayon ball swabs expire within seven (7) days from the date they are removed from the vendor packaged plastic wrap and the firm does not document the traceability of these swabs through documentation of vendor expiration dates.

G. SOP # 2MFG-002.17: Cleaning Procedures for Processing Equipment that describes the preparation of in-house cleaning agents (diluted [redacted] is inadequate because the preparation of this cleaning agent is not documented. A batch record with manufacturing instructions, lot numbers and expiration date have not been established for this process.

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
1431 Harbor Bay Parkway Alameda, CA 94502-7070 (510) 337-6700 Fax:(510) 337-6702 Industry Information: www.fda.gov/oc/industry	01/08/2013 - 02/28/2013* FEI NUMBER 3004182921

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Chungchiang Hsu, President & Chief Executive Officer

FIRM NAME	STREET ADDRESS
Impax Laboratories, Inc.	31145 San Antonio Street
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Hayward, CA 94544-7905	Drug Manufacturer

OBSERVATION 6

Batch production and control records do not include complete information relating to the production and control of each batch.

Specifically,

A. Start and stop times for critical process parameters (CPP) are not recorded in the batch record during production operation. For example, the start and stop time is not documented for Pyridostigmine Br CPP during pre-blending and final blending that affect blend uniformity.

B. API Assay results are not always used to calculate the amount of active ingredient needed to manufacture a given batch of drug products. For example, during the manufacture of Pyridostigmine, Tamsulosin, Colestipol, Carprofen, Fludrocortisone, Primidone, Promethazine, Fenofibrate, Dipyridamole, Galantamine, Terbutaline, and Oxybutynin; the amount of active ingredient to add during manufacturing is determined by a theoretical value of [redacted] and not the actual potency value.

C. There is a failure to maintain raw data during in-process parameter checks for tablet hardness and thickness. For example, all batch records and process validations reviewed during the EI do not have raw data printouts for hardness and thickness.

OBSERVATION 7

Reports of analysis from component suppliers are accepted in lieu of testing each component for conformity with all appropriate written specifications, without establishing the reliability of the supplier's analyses through appropriate validation of the supplier's test results at appropriate intervals.

Specifically,

The firm does not perform testing of raw materials for conformity with all written specifications reported on the vendor's Certificate of Analysis (COA). They only perform limited testing and have not established the reliability of the supplier's test results. The firm has no documented justification for not performing all tests listed on the certificate. For example:

Pertaining to NDA 203312 Levodopa/Carbidopa IPX066

A. For Carbidopa lots [redacted] used to manufacture NDA lots [redacted] the firm has not performed [redacted]
The firm has not established the reliability of the vendor's analyses for this test.

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B. For Levodopa lots [redacted] used to manufacture NDA lots [redacted] the firm has not evaluated the presence of the [redacted] The firm has not established the reliability of the vendor's analyses for this test.

C. For [redacted] manufacturer used in the submission, NDA 203312, the firm did not perform tests such as [redacted] The firm has not established the reliability of the vendor's analyses reported on the COA for these tests.

D. For [redacted] used in the submission lots, NDA 203312, the firm did not perform tests such as [redacted] as reported on the manufacturer's COA. The firm has not established the reliability of the vendor's analyses reported on the COA for these tests.

E. For [redacted] manufacturer's lots [redacted] respectively, the firm did not perform the [redacted] The firm has not established the reliability of the vendor's analyses reported on the COA for these tests.

OBSERVATION 8

Drug products are not stored under appropriate conditions of humidity so that their identity, strength, quality, and purity are not affected.

The firm stores hygroscopic drug products, such as Pyridostigmine and Colestipol, in warehouse [redacted] and warehouse [redacted] without establishing control limits and monitoring procedures to prevent product degradation from moisture.

OBSERVATION 9

An annual report did not include a full description of the manufacturing and control changes not requiring a supplemental application, listed by date in the order in which they were implemented.

Specifically,

A. SOP has not been established describing or referencing the criteria for filing changes being effected (CBE) or prior approval supplement submissions.

B. Change in humidity specification from [redacted] RH to [redacted] RH during production for Pyridostigmine was not addressed in a Changes Being Effected (CBE) submission or in the 2004 Annual Report submission to the Agency. Pyridostigmine is a hygroscopic drug product.

C. Change in final blending time from [redacted] minutes to [redacted] minutes during production of Pyridostigmine was not addressed in a Changes Being Effected (CBE) submission or in the 2004 Annual Report submission to the Agency. The increase in blend time was changed to improve blend uniformity.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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Impax Laboratories, Inc.	31145 San Antonio Street
CITY, STATE, ZIP CODE, COUNTRY Hayward, CA 94544-7905	TYPE ESTABLISHMENT INSPECTED Drug Manufacturer

OBSERVATION 10

Procedures describing the warehousing of drug products are not followed.

Specifically,

SOP 2WHC-004.14: Staging & Allocating Manufacturing Materials in Section 4.3 states that the electronic enterprise resource planning system is used to document the location, transfer and movement of materials in the warehouse.

On 1/10/2013, we requested printouts from the electronic enterprise resource planning management system. The status and location of [redacted] drums of raw material Copovidone lot 0000000881 that were stored in the warehouse were unaccounted for in the electronic enterprise resource planning management system.

REPEAT OBSERVATION

OBSERVATION 11

Written procedures are not followed for evaluations done at least annually and including provisions for a review of complaints, recalls, returned or salvaged drug products, and investigations conducted for each drug product.

Specifically,
SOP 2QUA-040.06: Annual Product Review that describes the review and approval of APR states in Section 5.1.5 that annual product reviews will be completed within [redacted] months after the end of the review period. This procedure is not followed. For example on [redacted] the most recent annual product review (APR) for Bupropion Hydrochloride Extended Release 100mg between [redacted] was not complete (approximately [redacted] months after the due date).

OBSERVATION 12

Employees engaged in the manufacture and processing of a drug product lack the training and experience required to perform their assigned functions.

Employees involved in all aspects of production and analytical testing of drug products are not adequately trained to perform their duties, see OBS 1-11.

*** DATES OF INSPECTION:**
01/08/2013(Tue), 01/09/2013(Wed), 01/10/2013(Thu), 01/11/2013(Fri), 01/12/2013(Sat), 01/14/2013(Mon), 01/15/2013(Tue), 01/16/2013(Wed), 01/17/2013(Thu), 01/18/2013(Fri), 01/19/2013(Sat), 01/21/2013(Mon), 01/22/2013(Tue), 01/23/2013(Wed),

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