DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
300 River Place, Suite 5900 Detroit, MI 48207 (313) 393-8100 Fax:(313) 393-8139 Industry Information: www.fda.gov/oc/industry	03/11/2009 - 05/12/2009 FEI NUMBER 1833173

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Daniel H. Movens, CEO

FIRM NAME	STREET ADDRESS
Caraco Pharmaceutical Laboratories, Ltd.	1150 Elijah Mccoy Dr
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Detroit, MI 48202-3344	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:

Note: All redactions are under FOIA exemption (b)(4).

MATERIALS SYSTEM

OBSERVATION 1

Records fail to include an individual inventory record of each reconciliation of the use of each component with sufficient information to allow determination of any associated batch or lot of drug product.

A. [redacted] Digoxin, USP, API Lot No. [redacted] was dispensed from 1/09/09 to 1/12/09. On 1/13/09, 1.352 Kg of lot [redacted] could not be located. To date, records do not indicate the disposition of the missing 1.352 Kg.

B. Metformin HCl, API Lot No. [redacted], on 8/25/08, 15 Kg could not be located in the warehouse. The investigation (IR 08-793) was closed on 9/22/08 with the conclusion that operators combined different receiving numbers of the same product. To date, records fail to account for the 15 Kg of Metformin Lot No. [redacted]

OBSERVATION 2

Written procedures are not followed for the storage and handling of components.

SOP [redacted]" was not followed to assure sufficient quantities of raw materials were available, as designated by your inventory tracking system [redacted]), and the return of any excess.

A. For raw materials not in a specified warehouse location, the quantity given to Dispensing is not documented on the Summary Pickup list. Examples include:

Item Name	Lot #	Receiving #	Qty Given to DISP

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Daniel J. Brown, Chemist Daniel J Brown
Rebecca E. Dombrowski, Investigator R E Dombrowski
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Tramadol	[redacted]	[redacted]	"Not in LOC"
Metformin	[redacted]	[redacted]	"Not in location"
Digoxin	[redacted]	[redacted]	"DISP"
Digoxin	[redacted]	[redacted]	"DISP"

B. Sufficient quantities of the following raw material were not given to Dispensing, as indicated on the Summary Pickup List generated by [redacted]. Examples include:

1. [redacted] Receiving No. [redacted] for Paroxetine [redacted] Lot No. [redacted] and [redacted]

2. Citalopram Receiving [redacted] For Citalopram [redacted] Lots [redacted]

C. Failure to document the return of excess raw materials for the following batches. Examples include:

Metoprolol [redacted] batches [redacted] Tramadol batches [redacted], Metformin [redacted] batch [redacted], and Citalopram batches [redacted].

OBSERVATION 3

There is a failure to thoroughly review any unexplained discrepancy whether or not the batch has been already distributed.

A. Investigation conducted under "NOE, Incident #09-005" dated 1/6/09 regarding [redacted] individual raw material batches with OOS inventory reconciliations, was found to be incomplete in the following instances:

1. Metoprolol Tartrate USP, lot [redacted] missing 2.61 Kg, thought to be incorrectly used in place of a different lot, but lacked evidence supporting this conclusion.
2. Carbamazepine USP, lot [redacted], missing 1.27Kg, believed to be incorrectly used in place of a different lot, but lacked evidence supporting this conclusion.
3. Carvedilol, lot [redacted], and [redacted] found with excess 4.268Kg and 10.379 Kg, believed a third raw material batch was dispensed in their place and was inaccurately documented. Investigation lacked documented evidence that such a switch had occurred.
4. Tramadol HCl API, lot [redacted], found with excess 2.405 Kg thought to be a result of rollover from previous lots dispensed and incorrectly documented but lacked documentation to support this conclusion
5. Metoprolol Tartrate USP, lot [redacted] found to contain an excess of 2.756 Kg was not investigated.

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B. Citalopram Hydrobromide API assigned lot number [redacted] was dispensed on 11/10/08 and again on 11/13/08 at which time 17.946 Kg could not be located. From 11/13/08 - 1/4/09 this missing quantity of 17.946 Kg was not investigated.

C. Meloxicam (Micronized) API assigned lot number [redacted] was dispensed on or about 8/13/08. On 10/3/08 0.492 Kg could not be found and an entry into [redacted] of "MATERIAL NOT IN LOCATION" was made. From 10/3/08 - 1/6/09 this missing quantity was not investigated.

D. [redacted] Tizandine Hydrochloride API lot 81161 was last dispensed 8/25/08 at which time an inventory of 0.868 Kg remained. On 9/14/08 it was noted that this remaining inventory could not be located, however investigation did not occur until 1/5/09.

E. Clozapine [redacted] API lot [redacted] was noted on 10/20/08 to have 2.821 Kg missing and an entry in [redacted] of "UNABLE TO LOCATE MATERIAL" was made. This missing quantity was not investigated until 1/2009.

OBSERVATION 4

Written procedures are lacking which describe in sufficient detail the receipt, identification, storage, and handling of components.

Written procedures do not describe in sufficient detail the designation or employee responsibilities relating to drug components in the "FRSH" or "DISP" locations, which are not physical warehouse locations.

A. [redacted] Digoxin, USP ([redacted] Lot # [redacted] was documented in [redacted] to be in the "FRSH" location between 10/13/08 to 1/26/09 and was dispensed during this time period.

B. [redacted] Digoxin, USP ([redacted]) Lot # [redacted] was documented in [redacted] to be in the "FRSH" location between 12/30/08 to 2/4/09 and was dispensed during this time period.

C. [redacted] Digoxin, USP ([redacted]) Lot # [redacted] was documented in [redacted] to be in the "FRSH" location between 9/15/08 to 9/26/08 and was dispensed during this time period.

D. [redacted] Tizanidine Hydrochloride lot [redacted] was documented in [redacted] to be in the "DISP" location 7/18-18/08 and was dispensed during this time period.

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PRODUCTION SYSTEM

OBSERVATION 5

Control procedures are not established which monitor the output and 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.

A. The following lots were sorted for tablet defects after in process controls and compression related issues were noted:

1. Digoxin 0.125 mg Tablets, USP lot 81404 was compressed 9/19-22/08 and sorted under SPO[redacted] for noted thick and soft tablets. The sort resulted in the rejection of[redacted] Tablets.

2. Digoxin 0.125 mg Tablets, USP lot 81401A was compressed 6/14-20/08 and sorted under SPO[redacted] for thick and thin tablets observed during packaging.

3. Clonazepam 0.5mg Tablets, USP lot 81529A was compressed 7/17-21/08 and sorted under SPO[redacted] for thin, soft, broken, and imperfect appearance tablets following observation of the same during packaging.

4. Clonazepam 0.5mg Tablets, USP lot 81534A was sorted under two Special Processing Operation orders [SPO[redacted] (8/19/08) and SPO[redacted] (11/11/08)] following the observation of thin tablets during packaging.

5. Clonazepam 0.5 mg Tablets, USP lot 81597A was sorted under Special Processing Operation order [SPO[redacted](9/4/08)] following the observation of thin tablets during packaging.

6. Clonazepam 0.5 mg Tablets, USP lot 81532 was sorted under Special Processing Operation order [SPO[redacted] (8/8/08)] following the observation of thin tablets during packaging.

7. Metoprolol Tartrate 50mg Tablets, USP lot 80345 was compressed 3/12-14/08 and sorted under[redacted] for noted thin and soft tablets.

8. Metoprolol Tartrate 50 mg Tablets, USP lot 82496 was sorted under two Special Processing Operation orders[redacted] (11/10/08) and[redacted] (11/18/09)] following the observation of broken tablets, thick tablets and black spots during compression and again during packaging.

9. Metoprolol Tartrate 50 mg Tablets, USP lot 81786 was sorted under Special Processing Operation order[redacted] (08/20/08)] following the observation of soft tablets and imperfect appearance during packaging.

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10. Metoprolol 50 mg Tablets USP lot 81102A was sorted under Special Processing Operation order [redacted] (6/18/08)] following the observation of thick tablets during packaging.

11. Metoprolol 25mg Tablets USP lot 80667A was sorted under Special Processing Operation order [redacted] (5/14/08)] following the observation of thick tablets during packaging.

12. Mirtazapine 30 mg Tablets, USP, lot 81126 was compressed beginning 06/02-04/08 and sorted under [redacted] for tablets with imperfect appearance.

B. The following un-sorted lots were the subjects of complaints relating to compressed tablet defects. The batch record for each of the following noted compression issues during production:

1. Metoprolol Tartrate 50mg Tablets, USP Lot 80959 was compressed 4/23-30/08 and received complaint COM[redacted] on 09/03/08 for tablet size variation.

2. Metoprolol Tartrate 25 mg Tablets, USP Lot 81739A was compressed 8/26-28/08 and received complaint COM[redacted] on 1/29/09 for tablet size variation.

3. Metoprolol Tartrate 50 mg round Tablets USP Lot 82036A was compressed 9/8-9/08 and received COM[redacted] on 1/28/09 for tablet size variation (thick).

4. Metoprolol Tartrate 25 mg Tablets, USP lot 80658A was compressed 4/11-14/08 and received COM[redacted] on 6/16/08 for tablet size variation (thick).

5. Metoprolol Tartrate 25 mg Tablets, USP lot 82695A was compressed 12/26-30/08 and received COM[redacted] on 3/12/09 for tablet size variation (thick).

6. Digoxin 0.125 mg Tablets, USP lot 81020A compressed 5/24-6/2/08 and received COM[redacted] on 11/10/08 for tablet size variation (thick).

7. Digoxin 0.125mg Tablets, USP lot 80771A compressed 5/1 - 6/08 and received COM[redacted] on 7/2/08 for tablet size variation (thick).

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OBSERVATION 6

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

A. In process tablet weights as recorded in the Batch Record are not always reflective of actual in process weights obtained. For example, tablets weighing [redacted] were obtained during in process checks of Metoprolol Tartrate, 50mg Tablets, USP, lot 80345, however these values are not recorded in the Batch Record. The tolerance range for Metoprolol Tartrate, 50mg, USP in process weights as specified in the Master Batch Record is [redacted] to [redacted].

B. SOP[redacted], was not followed during the dispensing of inactive raw materials Lactose [redacted], NF, [redacted] with Lactose [redacted], NF, [redacted]
1. "Operators failed to perform proper verification of materials prior to the dispensing process".
2. Sufficient quantities of [redacted] was not given to Dispensing.
3. Source containers were not scanned.

C. Clozapine Tablets, USP, 100mg, lot 80849 was dried for [redacted]. Batch instructions require [redacted] of drying and SOP [redacted] and [redacted]', permits continued drying at [redacted] increments until the desired [redacted]) is achieved. Drying in additiona[redacted] increments did not occur for this lot.

D. Batch Manufacturing Record compression instructions, '[redacted]" was not followed during compression of Metoprolol Tartrate, Tablets, USP, 25 mg lots. Four of four lots reviewed lacked documentation that this check had been performed. Examples: 80658, 80667, 81739, and 82695.

E. Review of the Batch Manufacturing Record compression section for Clonazepam Tablets, USP, 0.5 mg lot 81534 revealed the in-process hardness tests conducted between containers [redacted] and [redacted] resulted in five consecutive OUT OF CONTROL and OUT OF TOLERANCE test results on 8/14/08. Review of the Compression Parameters Record Sheet finds no documented adjustments nor indication of hardness problems.

F. SOP[redacted], was not followed in the handling of excess quantities of raw material. IR 08-793, Dated 8-25-08 was initiated after [redacted] showed 15kg of Metformin HCl active raw material, Lot No. [redacted], could not be located in the [redacted] Warehouse. The root cause was reported to be operators combining small amounts of one receiving number with another receiving number, which caused the stock of Metformin HCl, in [redacted], to become out of acceptable limits.

G. According to SOP[redacted]', the [redacted] result printout ticket for this lot is to be recorded with product specific information

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including product name, lot number, part lot number, and number of hours of total drying at the time of the test. The [redacted] printout ticket for Clozapine Tablets, USP, 100mg, lot 80849 is recorded as [redacted]", though it is reflective of drying after [redacted] active drying and [redacted] of air drying.

H. There is no documentation to support QA approval to proceed when temperatures in the compression room exceeded [redacted] on 7 occasions during compression of Metoprolol Tartrate, 50mg Tablets, USP, lot 80345 as required per production Batch Record instructions.

OBSERVATION 7

Batch production and control records do not include the weights and measures of components used in the course of processing each batch of drug product produced.

Specifically,

Master Batch Records do not contain complete weight records of dispensed material for the following:

A. Digoxin Tablets, USP, 0.25mg, Lot No. 90018

B. Lactose Anhydrous, NF, Supertab 21AN, Lot No. [redacted] dispensed for Paroxetine Lot #82576

OBSERVATION 8

Time limits are not established when appropriate for the completion of each production phase to assure the quality of the drug product.

a- End limits on drying have not been established for the drying of Clozapine Tablets, USP, 100mg. For example, during [redacted] of lot [redacted], [redacted] of active [redacted] drying occurred, with an additional [redacted] of [redacted] inside the [redacted] The Batch Manufacturing Record for Clozapine requires [redacted] of drying, though no end limit is specified. There is no data to support the acceptability of this [redacted] after [redacted] of [redacted] in addition to the [redacted] experienced by this lot.

b- Time limits have not been established for the rate of addition of [redacted] material to the [redacted] used in

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[redacted]Digoxin[redacted]n (for 0.125mg tablets, USP) as observed in the completed batch record, lot 81404. [redacted] are recorded by operators performing this operation in the batch record. Different rates of addition were stated to affect [redacted] of the [redacted] material.

OBSERVATION 9

Deviations from written production and process control procedures are not justified.

Specifically,

Performance Qualification of the [redacted], asset # [redacted] observed in use in metal detecting CMT lot 90131 was found inconsistent with routine metal detection use in that the challenge pucks used to determine proper functioning of the unit prior to use, and consistent with current practice as observed on 3/16/09, are not the same sizes as those used in the Performance Qualification of this same asset.

QUALITY SYSTEM

OBSERVATION 10

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

Specifically,

A.Change control record, CR 08-317, a permanent change reflecting the batch charge calculations of active and inactive materials, did not fully evaluate the batch impact of the change prior to implementation according to SOP [redacted]. Specifically, the dispensing of Digoxin, USP, active pharmaceutical ingredient, for Digoxin Tablets, USP, 0.125mg LOT 81404, under this Change Control resulted in [redacted] dispensed containers of the material instead of the required [redacted] dispensed containers per the Batch Master Record.

B. SOP1[redacted] was not followed in that training was not conducted "in a timely manner" and any documented extension was not requested until 3 months past the due date. CAR 08-030 issued 5/15/08, CAR 08-043 issued 5/22/08, CAR 08-048 issued 6/12/08, and CAR 08-110 issued 8/27/08, were held until 11/7/08 when training for compression personnel on the proper tablet press setup, cleaning of tablet presses, and feeder platform set up deemed to prevent repeat issues of metal contamination, black spots and thick and thin tablet issues noted in manufactured Rx drug products. Likewise CAR08-074 issued 6/13/08 was held until 2/10/09 when training for compression personnel on the set up checklists after Type 1 and Type 2 cleaning were held. Examples include: Metoprolol Tartrate USP

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lot 81560, Clonazepam 0.5 mg lot 81597, Clonazepam 0.5 mg lot 81532

C. SOP [redacted]", was not followed in that, per section [redacted] an effectiveness check of CAPA record, CAR 08-038 (pertaining to the removal of the tablet de-duster during compression set-up and troubleshooting) , dated 5/26/08 was not requested or performed though monitoring of the CAPA through incidents and complaints was possible.
Specifically, Clonazepam 0.5mg Tablets, USP lot 81529 received a complaint and Metoprolol Tartrate 50mg, USP, lot 81102 was the subject of an incident after implementation of CAR 08-038. Both investigations reference the [redacted]

D. SOP [redacted] was not followed in that
Approval by the Director of Technical (or designee) was not obtained for the compression of Metoprolol Tartrate, 50mg tablets, USP lot 80959 using the [redacted] prior to actual batch compression. Specifically, Change Control request, CR 08-219, to allow for the compression of Metoprolol Tartrate, 50mg tablets, USP using the [redacted] was not approved prior to use in compression activities. This change control was originally initiated and approved for [redacted] lots of Metoprolol Tartrate, 50mg tablets, USP (not including lot 80959).

E. A QA Hold was not placed on Citalopram HBr Tablets, 10mg, lot 80795A, subject to Special Processing Operation, SPO-08-491 as required per SOP [redacted]

F. SOP [redacted], was not followed to ensure batches are not released for distribution prior to closure of an incident. Specifically, IR09-067, in which 1.352kg of [redacted] Digoxin, USP, lot 82855, was missing from the [redacted] Warehouse. The final Digoxin Investigation list provided on 4/7/09 contains [redacted] lots associated in IR 09-067, of which, 102 lots were indicated to have been released into distribution.

G. SOP [redacted] does not describe the procedure for 100% inspection.

1.On 3/16/09, an operator was observed inspecting a large pile of Metformin HCl Tablets, USP, 500mg, Lot No. 82742, in a scoop rather than a clear inspection tray.

2. On 3/16/09 we observed an operator inspecting Allopurinol Tablet lot 90260 using a scoop rather than the inspection tray reportedly called for.

H. SOP [redacted] does not describe the procedure the QA specialist should follow when performing the visual AQL inspections. On 3/12/09, Digoxin 0.25mg tablets, Lot #90187, was being sorted according to [redacted] for black specks. The QA specialist was observed scooping tablets with gloved hands and inspecting the tablets in her palm for all possible critical, major and minor defects, including but not limited to, size variation and soft/low weight tablets.

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OBSERVATION 11

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

The investigation of 1.352kg of missing [redacted] Digoxin, USP, Lot No. [redacted], IR 09-067, did not extend to all other drug products that may have been associated with the incident.

OBSERVATION 12

Individuals responsible for supervising the processing of a drug product lack the training and experience to perform their assigned functions in such a manner as to assure the drug product has the safety, identity, strength, quality and purity that it purports or is represented to possess.

Citalopram HBr Tablet 40 mg lot 81940A was released and distributed after a newly trained QA Supervisor reportedly was confused and released this lot based on the in-process [redacted] results, dated 9/16/08, and not based on the final product analysis report dated 12/5/08 which reported failed dissolution results.

OBSERVATION 13

Written records of investigation of a drug complaint do not include the findings of the investigation and the follow-up.

Specifically,

Complaint investigations into the following were not completely evaluated. For example:

A.Digoxin 0.125mg Tablets, USP, lot 81404 was the subject of both a complaint and an ADE as follows:

1. Complaint 08-176 was received on 12-04-08 for size and appearance variation. Retain samples (R1, R2, and R3) were evaluated noting: 19, 13, and 26 tablets from each bottle respectively with "Size Variation". There is no record that the 58 isolated tablets with size variation were further weighed or analyzed before the complaint file was closed 1-15-09.

2. ADE 08-184 was received on 11-10-08, and involved hospitalization, with both labeled and unlabeled events reported.

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NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Daniel H. Movens, CEO

FIRM NAME	STREET ADDRESS
Caraco Pharmaceutical Laboratories, Ltd.	1150 Elijah Mccoy Dr
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Detroit, MI 48202-3344	Drug Manufacturer

QC Testing of retain samples revealed the potency of selected individual tablets ranged from [redacted] to [redacted] of the labeled claim of the Digoxin 0.125mg tablets, USP.
No Health Hazard Evaluation on the effect of consuming tablets with individual assay values of [redacted] to [redacted] was performed on this marketed lot prior to the closing of this ADE investigation file on 1-23-09 with QA/RA confirmation on 3/02/09.

B. Digoxin 0.125mg Tablets, USP, lot 80771A was the subject of both a complaint and an ADE as follows:

Adverse Drug Event #08-101 was received on 7/1/08 from a patient who experienced increased seizures, lips tingling, lightheadedness, and difficulties concentrating 2-3 weeks after taking this drug. Complaint #08-094 was received on 7/2/08 due to large tablets. An investigation was conducted and [redacted] of [redacted] complaint sample tablets was out of tolerance for high weight. No action was taken as a result of the OOT finding. The complaint file was originally closed on 9/4/08.

C. Complaint #08-149 was received on 9/30/08 for Clonazepam 0.5mg tablet Lot #81529A due to variation in tablet size. Retain samples were evaluated (R1, R2, and R3) which noted one tablet in R3 was out of tolerance for low weight. Complaint samples were evaluated: 3/9 tablets were OOT for low weight and [redacted] tablets were OOT for low thickness. No further action was taken as a result of the OOT findings. The complaint file was originally closed on 11/10/08.

D. Complaint COM 08-095 was received 7-02-08 for oversized Mirtazapine 30mg tablets, USP from lot 72694A. Specifically, the complainant indicated that "5 tablets in the bottle were larger and they jammed the equipment". An evaluation of the complaint sample revealed that 3 units were out of tolerance for weight as specified in the Batch Master Record. No further action was taken as a result of the findings as listed above.

E. Clozapine Tablets, 100mg USP, lot 80849 was the subject of 3 complaints (08-079, 08-080, 08-120) within 2 months (6-7/2008) for broken tablets in this finished product. The complaint investigations resulted in a review of the retained samples for this lot, and the isolation of a broken tablet and 3 chipped tablets. A batch record review was also performed indicating that [redacted] of excess drying was incurred during drying of this lot as a result of a power failure. The written investigation into each of the 3 complaints fails to address the excess drying, and any further analysis of the retained samples as a result of the chipped and broken tablet findings.

F. Complaint COM 08-083 dated 6/16/08 for Metoprolol Tartrate 25 mg Tablets lot 80658A for oversized tablets was the 11th of 14 events associated with tablet press [redacted]. A problem with the scraper was documented at the beginning of the run. Returned samples were found to exceed Caraco's weight and thickness tolerances by over [redacted]. Retain samples were pulled on 7/24/08 (80658A) and again on 8/6/08 (80658B). Addendums were added to the investigation on 12/16/08 and on 2/12/09.

G. Complaint COM 08-169 dated 11/20/08 for Metoprolol Tartrate 50 mg Tablets lot 81786A for oversized tablets was the 5th Metoprolol complaint, the 15th overall complaint and the 8th incident for press [redacted] related to size received in 2008. Five hardness adjustments were made during the compression of this lot and a portion of this lot was subject of a 100% visual

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inspection due to soft and imperfect tablets being present. A returned complaint tablet was documented as outside Caraco's thickness range.

H. Complaint COM 09-006 dated 1/29/09 for Metoprolol Tartrate 25 mg Tablets lot 81739A for oversized tablets was the 12th of 14 events associated with tablet press #28840128. Problems with the feed frame were documented at the beginning and the middle of the run. The complaint sample weighed well in excess of Caraco's upper tolerance.

OBSERVATION 14

Procedures are not established which are designed to assure that the responsible officials of the firm, if they are not personally involved in or immediately aware of such actions, are notified in writing of investigations conducted.

Specifically,

SOP [redacted], did not assure the responsible officials were notified of investigations. IR 09-067 in which 1.352 kg of [redacted] Digoxin, USP, Lot No [redacted], was missing from the warehouse. An initial search was conducted on 1/13/09. An Incident Initiation Investigation Tracking Sheet was not generated until 1/30/09.

OBSERVATION 15

Records are not maintained so that data therein can be reviewed at least annually to evaluate the quality standards of each drug product to determine the need for changes in specifications or manufacturing or control procedures.

Specifically, requests for annual product review for Digoxin Tablets USP, Metoprolol Tartrate Tablets USP and Carbamazepine Tablets USP revealed only the year 2007 reviews were available in March 2009.

FACILITIES AND EQUIPMENT

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OBSERVATION 16

The building lacks adequate space for the orderly placement of equipment and materials to prevent mix-ups between different components and in-process materials and to prevent contamination.

Specifically, Raw material warehouse facility ([redacted]) did not have adequate storage available for all of its raw materials and in-process ([redacted]) materials. For example:

A [redacted] Digoxin lot [redacted] was in location "FRSH" (Fresh) without a specific location designated for the warehouse from 10/13/08 to 1/26/09

B [redacted] Digoxin lot [redacted] was in location "FRSH" (Fresh) without a specific location designated for the warehouse from 12/30/08 until it was reported missing.

C. [redacted] Digoxin lot [redacted] was in location "FRSH" (Fresh) without a specific location designation for the warehouse from 9/15/08 to 9/26/08.

D. Baclofen, USP - [redacted] lot [redacted] was in location "DISP" (Dispensing) without a specific location designated for the warehouse from 4/22/08 through 7/25/08.

E. Metoprolol Tartrate, USP lot [redacted] was in location "DISP" (Dispensing) without a specific location designated for the warehouse from 5/15/08 through 9/25/08.

OBSERVATION 17

Equipment used in the manufacture, processing, packing or holding of drug products is not of appropriate design to facilitate operations for its intended use.

Specifically, temporary change control no. 08-1009 dated 9/19/08 was approved to allow for the compression of [redacted] lots of Digoxin Tablets using the [redacted] tablet press as an alternate tablet press for Digoxin Tablets, USP, 0.25 mg without a process verification to determine whether such a change would have an adverse effect on the finish tableted product. For example [redacted] of the [redacted] lots, 81819A was subject of a [redacted] after finding soft and thick tablets.

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OBSERVATION 18

Written procedures for cleaning and maintenance fail to include parameters relevant to the operation.

Specifically,

On 3/16/09, written procedures did not exist for the storage and labeling of cleaning solutions and agents used in cleaning production equipment and containers. For example,

A. A large drum of an unlabeled solution was observed in the [redacted] wash rack area. This solution was stated to be for cleaning component container lids.

B. Two containers labeled [redacted] were observed in the [redacted] wash rack area; one container contained a clear, colorless solution and the second contained a blue solution. Confirmation of the identity of the blue solution was not provided.

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