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	03/03/2009 - 03/26/2009* FEI NUMBER 3003693105

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Steve R. Klemm, Chief Operating Officer

FIRM NAME	STREET ADDRESS
Corium International, Inc.	4558 50th St Se
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Grand Rapids, MI 49512-5401	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:

Observations are for the Fentanyl Transdermal System 25mcg/hr, 50mcg/hr, 75mcg/hr, and 100mcg/hr.

OBSERVATION 1

Failure to reject any lot of components that did not meet the appropriate written specifications for identity, strength, quality, and purity.

Specifically, incoming lot 703131 dated 3/09/07 for (b) (4) was not rejected. This material is a new grade which is currently approved for use in all batches. The material Certificate of Analysis for lot 703131 was reviewed and inspected by raw material inspectors. The inspection failed to identify discrepancies from previously received, approved, and validated lots of the raw material. Differences include the product name, place of manufacturing, change in weight format,and change in chemical specification listing format. The previous lot 412132 had been received on 12/17/04. Identification of these changes may have led to the failure of the incoming raw material lot. The changes were not identified and therefore the raw material was not rejected and was used to produce gel mix lots 27258 and 27259. Gel mix Lot 27258 was used to produce patches under (b) (4) Fentanyl 25 mcg/hr which failed during manufacturing due to large particles that clogged the slot die ((b) (4)). The patches from Lot 27258 (b) (4) , the remaining bulk gel mix for lot 27258, and the bulk gel mix of lot 27259 were rejected under (b) (4) dated 5/10/07 as a result of material insolubility during blending as a result of the raw material from lot 703131 being a different grade than had previously been received. The material from lot 703131was identified on the CoA differently then from the previous lot 412132 received on 12/17/04.

OBSERVATION 2

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

Specifically, modifications to the dispense settings, such as (b) (4) " and replacement of the slot die are not always documented in the production and control records. These dispense settings are changed during manufacturing operations to achieve proper gel placement and product quality. During manufacturing of lot 29057 (b) (4) for 25 mcg/hr a change was made to the slot die. This change was not recorded in the batch record.

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OBSERVATION 3

The master production and control records are deficient in that they do not include complete instructions and procedures.

Specifically,the manufacturing instructions(b) (4)), workmanship standards (b) (4)) and accompanying training manual(b) (4)) lack procedures by which the user should modify the dispense settings such as "(b) (4) ". These dispense settings are changed during manufacturing operations to achieve proper gel placement and product quality. Such changes can also have corrective not just preventative actions such as with lot 28446 which was manufactured into patches from 8/28/08 to 9/4/08. Under(b) (4) dated 11/21/08, it was noted that during the manufactuturing of lot 28446 the(b) (4) " speed was changed to correct a problem with stringing. The stringing was a result of the variation in viscosity of the gel and was creating heat seal defects.

OBSERVATION 4

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, there is not always documentation of additional in-process testing of units when changes are made to the operating settings. Controlled stops, for instances such as changes to the slot die or dispense settings are not recorded in the batch records. If these controlled stops result in the line being stopped for less than(b) (4) minutes, there are no additional samples collected and tested to assure the changes had no detrimental affect on the product. Normal sampling and testing of (b) (4) in-process samples are collected during the next scheduled(b) (4) minute in-process sample.

OBSERVATION 5

There is a failure to thoroughly review 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, rejected material is not always reviewed to determine a reason for rejection. Units that are manually rejected by (b) (4) on-line inspectors, are in some cases only visually counted by the off-line defect inspector. During instances of restarts such as after controlled stops for dispense setting changes and slot die replacement, the parts are rejected manually by the on-line inspector. These parts are printed by an ink jet to identify them as having been manually rejected. There is no visual inspection of these rejected units for failures. During manufacturing on 3/4/09 of Fentanyl Transdermal Patches Lot 29057 for 25mcg/hr, after a controled stop for a slot die change, material was rejected by the on-line inspector and identified with ink jet printing. The rejected material was counted and placed into an "(b) (4) " bag by the off-line defect inspector, but was not visually inspected to look for failures.

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OBSERVATION 6

The suitability of all testing methods is not verified under actual conditions of use.

Specifically, procedure (b) (4) ' which is used to test the viscosity of raw material and in process Fentanyl gel mix has not been tested by the firm to establish its accuracy and reliability in the lab on site.

OBSERVATION 7

In-process specifications are not determined by the application of suitable statistical procedures where appropriate.

Specifically, the firm's in process specifications for viscosity measurements were based on the average of all viscosity samples (b) (4) batches with (b) (4) samples each and (b) (4) batches with one sample each). All samples were counted equally instead of properly weighting the (b) (4) samples for the first (b) batches as (b) (4) of a data point.

In addition, there is no written justification as to why (b) (4) was a reasonable viscosity range.

OBSERVATION 8

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

Specifically, DEV (b) (4) dated 10/28/08 lot 28469 which was opened for no recorded downtime (b) (4) dated 2/3/09 for lot 28993 which was opened for bubbles in the heat seal, and (b) (4) dated 2/6/09 lot 28993 which was opened for bubbles in the heat seal were all voided out and determined to warrant a Deviation or Non Conformance by Quality Assurance. The reason for Quality Assurance's justification for not investigating the Deviation and Non conformance was not documented.

OBSERVATION 9

Laboratory records do not include a statement of each method used in the testing of a sample and the location of data that establish that the methods used in the testing of the sample meet proper standards of accuracy and reliability as applied to the product tested.

Specifically, there is no statement on laboratory procedure (b) (4), which is used to test the viscosity of raw material and in process Fentanyl gel mix, identifing which method (such as USP) is used in the testing of viscosity.

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*** DATES OF INSPECTION:**
03/03/2009(Tue), 03/04/2009(Wed), 03/05/2009(Thu), 03/06/2009(Fri), 03/10/2009(Tue), 03/11/2009(Wed), 03/12/2009(Thu), 03/13/2009(Fri), 03/17/2009(Tue), 03/24/2009(Tue), 03/26/2009(Thu)

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