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	09/15/2008 - 11/07/2008
	FEI NUMBER 1811666

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: John T. Hendrickson, Executive Vice President of Global Operations & Supply Chain

FIRM NAME	STREET ADDRESS
L. Perrigo Co.	515 Eastern Ave
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Allegan, MI 49010-9070	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

Drug product production and control records, are not reviewed by the quality control unit to determine compliance with all established, approved written procedures before a batch is released or distributed.

A. Two lots of Sleep Aid Tablets (Doxylamine Succinate Tablets, 25 mg - ANDA (b) (4)) lot numbers 8EE0802 and 8JE0699 were assigned an unapproved 36 month expiration date and released.

B. Multiple lots of Naproxen Sodium 220 tablets (10 lots) and caplets (25 lots) were assigned an unapproved 48 month expiration date and released. Examples include: 8GE0281 and 8GE0304

C. Three lots of APAP 500 mg Gelcaps were assigned an unapproved 48 month expiration date and released. Examples include: 8GE0488, and 8GE0745

OBSERVATION 2

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

A. The following lots of Natural Senna Laxative Tablets, manufactured by (b) (4) . failed stability assay and remain on the market:

1. Investigation of deviation (b) (4) , dated 10/29/2007, reported an OOS 3 month stability result for lot 7B0991. This investigation remained open and unresolved. The decision to recall was made 9/23/2008 by (b) (4) . This lot's expiration date is March 2009.

2. Investigation of deviation (b) (4) , dated 6/12/2008, reported OOS 9 month stability results for lot 7G0903. This investigation remains open and unresolved. This lot's expiration date is July 2009.

3. Investigation of deviation (b) (4), dated 8/23/2007, reported an OOS 9 month stability result for lot 6GE0670. The investigation into this issue remained open and unresolved. This lot expired 4/2008.

B. Investigation of (b) (4), dated 12/21/2007, reported failing release assay result obtained 10/31/2007 for Natural Senna Laxative Tablet, annual (2007) confirmation batch, lot 7E1788 manufactured by contract supplier (b) (4), Inc. remains open and unresolved. Lot 7E1788 is maintained in an on hold status and has not been rejected. Subsequently received lots were not tested prior to release/distribution. Examples 7K2058, 8A2470, and 8C1587

C. Investigation of deviation (b) (4) dated 3/28/2008, reported an OOS 18 month stability result for Chlorpheniramine Maleate Tablet lot 6F1641 manufactured by contract supplier JB Laboratories. This investigation remained open and unresolved. This lot 's expiration date is April 2010.

D. Investigation of deviation (b) (4) dated 7/31/2008, reported an OOS 24 month stability result for 81 mg Enteric Coated Aspirin tablet lot 6EE0500 manufactured by contract supplier (b) (4) This investigation remained open and unresolved. This lot expired March 2008.

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.

Investigations into two content uniformity failures and batch rejections experienced 4 months apart for APAP 160 mg Jr Grape Chewable Tablets were both inconclusive. A Project Plan Request was issued 6/18/08. To date no activities have been initiated.:

Lot #	Date	Assay Result	Specification
7B0254	3/11/07	Acetaminophen Content Uniformity Assay (b) (4)	(b) (4)
7F1074	7/1/07	Acetaminophen Content Uniformity Assay (b) (4)	(b) (4)

OBSERVATION 4

An NDA-Field Alert Report was not submitted within three working days of receipt of information concerning a failure of one or more distributed batches of a drug to meet the specifications established for it in the application.

Field Alert was not filed following a Quality Assurance error (deviation (b) (4)) which resulted in multiple lots of Naproxin Sodium Caplets and Naproxin Sodium Tablets being released labeled with expiration dating exceeding the 36 months filed in the application ((b) (4)) by 12 months (48 months). Examples include: Lot (b) (4)

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OBSERVATION 5

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

A. SOP (b) (4) entitled "(b) (4) " calls for investigation of any failed/OOS confirmation batches. It further calls for QA to determine "(b) (4) ". This did not occur for the batches of Natural Senna Laxative Tablets received following the 10/30/07 OOS results obtained for batch 7E1788. The investigation remained as "Draft" as of the start of this inspection.

B. SOP (b) (4) " was not followed with regard to compiling quality data on a quarterly basis for all external manufacturers. The following contract manufactured data were not compiled:

1. For (b) (4) evaluations for (b) (4) 2007 and (b) (4) of 2008 were all dated 9/23/08. (b) (4) manufactures the following drug products for Perrigo: Natural Senna Laxative Tablets; 81 mg enteric coated aspirin (Yellow and Peach); and 325 mg enteric coated aspirin.

2. For JB Laboratories quarterly evaluations for 4th quarter 2007 and 2nd quarter 2008 were both dated 9/22/08. JB Labs manufactures the following drug products for Perrigo: Alertness Aid, Chlorpheniramine Maleate Tablet, and APAP 500 mg Caplets.

3. For (b) (4) evaluations for (b) (4) 2008 were both dated 9/26/08. (b) (4) manufactures Loratadine D 10 mg and Loratadine 10 mg QD tablets for Perrigo.

4. In addition this SOP was not followed in that implementing corrective actions and improvements as necessary was not done. (b) (4) vendor quality evaluations show 18 and 100 advisories, respectively for the past (b) (4) , the majority concerning the condition of incoming shipping cartons of Omeprazole products. There was no written plan to ameliorate the problem.

OBSERVATION 6

The quality control unit lacks responsibility for approving or rejecting drug products manufactured under contract by another company.

Appropriate statistical controls were triggered and/or not used and product was released. For example,

A. For Chlorpheniramine Maleate Tablets from JB Labs, lot 7J1978, released with a (b) (4) assay although your internal alert limit is (b) (4)

B. For Chlorpheniramine Maleate from JB Labs, lot 6F1641exp. Date 4/2010, the OOS 18 month stability assay of (b) (4)

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was not predicted by (b) (4) " from the release assay of (b) (4)

C. 1. For Natural Senna Laxative Tablets from TCL, draft deviation investigation (b) (4) initiated 8/23/2007, represents the first of 4 deviation reports for stability or release testing that were Out of Specification for Total Sennosides or Uniformity of Dosage. The investigation describes a 6/6/08 decision whereby "(b) (4) ". However, distribution of previously received lots including (b) (4) continued through 8/25/08 or until gone.

C. 2. Similarly, subsequent to the 1/18/08 issuance of a change control order to reduce the expiration date of peach colored 81 mg Aspirin Enteric Coated Tablets, following several stability failures, 32 lots were released with 24 month expiration dating periods assigned. For example:

Package Size	Lot Number	Expiration Date	Dating Assigned	Dates Shipped
300 Count	7KE0619	6/18/2009	24 months	2/12,20/2008
300 Count	7HE0550	5/11/2009	24 months	2/6/2008

D. For yellow colored and for peach colored 81 mg Aspirin Enteric Coated Tablets from (b) (4) ., the Quality Unit has not acted on the Acid Test stability failures, between 18 and 24 months, experienced consistently since 2005. Lots currently on the market with expiration dating periods assigned that have been longer than 18 months are:

Package Size	Lot Number	Expiration Date	Dating Assigned
500 Count	7FE0096	1/15/2009	24 months
500 Count	7LE0379	7/13/2009	24 months
500 Count	7LE0263	6/24/2009	24 months
500 Count	7HE0128	4/28/2009	24 months
500 Count	6FE0217	2/28/2009	36 months
500 Count	6EE0115	2/17/2009	36 months
300 Count	6FE0101	2/28/2009	36 months
300 Count	6EE0118	2/25/2009	36 months
180 Count	6EE0806	2/10/2009	36 months
180 Count	7JE0530	5/29/2009	24 months
300 Count	7KE0619	6/18/2009	24 months
300 Count	7JV0522	5/1/2009	24 months
300 Count	7HE0550	5/11/2009	24 months
180 Count	7LE0962	8/19/2009	24 months
180 Count	7KE0368	6/18/2009	24 months
180 Count	7LE0374	6/18/2009	24 months
180 Count	7HE0052	5/11/2009	24 months

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OBSERVATION 7

The quality control unit lacks the responsibility and authority to reject all drug products.

Appropriate statistical controls were triggered and/or not used and product was released. For example,

A. The 4/29/08 packaging of tote (b) (4) of (b) (4) lot (b) (4), an AQL test for foreign particles was performed and was failed for particles. A deviation report showed that the result was overturned, the tote filled and released. Review of the (b) (4) Formula (b) (4), the source batch record, showed that the manufacturing batch was aborted and then begun again, and the cleaning/use log showed that there had been no cleaning done after the previous (b) (4) batch or during the manufacturing of the batch.

B. There was no explanation for the 10/1-12/31/07 APAP ER 650 mg Tablet formula (b) (4) within specification dissolution profile changes in (b) (4) of batches. In addition, the reason for the rejection of batch (b) (4) for which the immediate release tablet layer failed, was not determined.

OBSERVATION 8

Results of stability testing are not used in determining expiration dates.

Review of the Nicotine Lozenges stability indicating assay test method validation showed that 4 of 6 forced degradation were ineffective. The study did not adequately anticipate observed degradation in the drug product; for example, Nicotine 2 mg Lozenge batch #6GO998 failed for assay at 18 and 21 mo. (b) (4) Relative Humidity. For Investigation (b) (4) there was no reason given for the failure. And for deviation (b) (4) the 18 mo. stability failures for largest unknown impurity for this same lot under projec (b) (4) had no assignable cause. The deviation report stated that the current 24 mo. expiration dating period was justified by other data.

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OBSERVATION 9

Laboratory records do not include the initials or signature of a second person showing that the original records have been reviewed for accuracy, completeness, and compliance with established standards.

A. Black and white copies of raw weighing data for the impurity standards for stability testing of Cetirizine Tablets on 7/23/08 showed weight ticket lot numbers added in blue ink and these changes were not dated. These changes were made as the documents were previewed prior to FDA's review.

B. Microbiological raw data is placed directly into LIMS, with no check for accuracy.

OBSERVATION 10

For components removed from the original containers, the new container fails to be identified with component name or item code, receiving or control number, weight or measure, and batch for which component was dispensed including product name, strength and lot number.

A. On 9/15/08, a pallet holding two unidentified drums and several raw material containers was observed in a hallway between several work centers in Plant [redacted] tablet manufacturing.
Batch Record #8J2663 IM APAP ER MIX formula # (b) (4) was later identified as an aborted batch that had been the source of the pallet in the hallway. There was no note of the 9/8/08 discovery of foreign material during milling on the batch record, as required by standard operating procedure.

B. On 9/15/08, an otherwise unidentified box, with "MAG" handwritten on it, containing a bag of white powder was observed in a warehouse on a pallet with other raw materials. Batch record #8G0284 APAP ER Release Mix Formula (b) (4) was later identified as an aborted batch that had been the source of the pallet of goods. The 7/25/08 investigation into the metal found during Pregrind-1 was incomplete and did not include earlier batches for which the Pregrind#1 had employed the same (b) (4)

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FDA EMPLOYEES' NAMES, TITLES, AND SIGNATURES:

Patsy J Domingo, Investigator

Regina T. Brown, Investigator

Caroline H. Le, Investigator

SEE REVERSE OF THIS PAGE	This is a modified document.	DATE ISSUED 11/07/2008