Establishment Inspection Report	FEI:	**1911445**
Novartis Consumer Health	EI Start:	06/13/2011
Lincoln, NE 68517-9626	EI End:	07/08/2011
EMM, JRL		

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SUMMARY

(Written by EMM)

This inspection was directed to investigate concerns over continued NDA 3-Day Field Alerts regarding solid dosage form mix-ups for products manufactured at this site. The inspection was expanded to include the following systems: Quality, Production, Packaging and Labeling, Facilities and Equipment. There was minimal coverage of Materials or Laboratory Systems during this inspection.

The firm is an own-label and contract human and animal drugs manufacturer. CP 7356.002, Drug Manufacturing Inspections and CP 7371.001, Animal Drug Manufacturing Inspections, were used as guidance for this inspection. The FACTS assignment number for this inspection is 1295674.

The previous comprehensive inspection occurred 4/5-16/10 and was classified VAI.

A two-item FDA 483, Inspectional Observations, was issued due to failure to follow process control procedures for laboratory documentation excursions and not extending an investigation regarding these laboratory documentation excursions.

At the conclusion of this inspection, a 13-item FDA 483, Inspectional Observations, was issued to Mr. Terence J. Walsh, Site Leader. Deviations include: Quality Unit oversight failure, failure to open investigations when required, failure to extend investigations to other lots of product potentially affected (REPEAT OBSERVATION), failure to file 3-Day Field Alerts as required, failure to identify specific equipment used on non-dedicated packaging lines, failure of Quality Unit to review critical complaints since at least 2009, failure to identify root-cause of mix-up complaints, investigation conclusions are not supported by evidence, failure to review critical complaints in a timely manner, numerous instances of failure to follow procedures, inadequate number of personnel conducting complaint investigations and review, inadequate personnel training and incomplete equipment use logs.

No refusals were encountered during the inspection.

During this inspection, a voluntary recall from (b) (4) (a firm using Novartis to contract manufacture (b) (4)) was initiated due to problems identified at this facility. An NDA Field Alert was filed (b) (4) due to an issue of mixed tablets. This recall was initiated on (b) (4) for (b) (4) Lots: (b) (4) and (b) (4) .

Sample DOC 651311 This documentary sample was collected to document the interstate movement of active pharmaceutical ingredient Acetaminophen, USP, on 9/18/09. It was then manufactured into finished product (Excedrin Tension Headache Express Gels) on or about 11/3/09, and distributed into interstate delivery on 11/16/09. This lot of product received a complaint for "foreign product" found in container, which was thought to be Excedrin Tension Headache Caplets (See Exhibit **JRL 9, page 12** for photo of two products). The complainant's bottle was never returned, because it was never requested from the complainant. Investigation 92546 (**Exhibit JRL 15**) indicated Excedrin Tension Headache Caplet 50 count bottles were packaged on the same packaging line on 11/12/09 (1 day prior to the packaging of Excedrin Tension Headache Gelcaps, lot 10078599). The root cause or conclusion for this investigation had not been established. See Observation # 10B below for details.

Sample DOC 651310 This documentary sample was collected to document the interstate movement of raw ingredient, on 8/6/10. It was then manufactured into finished product (Excedrin Extra Strength Caplets) on 9/30/10, packaged on 10/4/10, and distributed into interstate delivery on 10/5/10. This lot of product received a complaint for "foreign product" found in container, which was confirmed to be Excedrin ES Gelcaps. Investigation 88510 (**Exhibit EMM-13**) indicated Excedrin ES Gelcaps were packaged immediately prior to the affected lot. The conclusion indicated there is a very small to no possibility that the foreign product was introduced through Novartis procedure and practices. The root cause of the mix-up was not determined. See Observation # 3B below for details.

The firm was warned of their responsibilities under the FD&C Act. Management stated they understood the deficiencies and promised a written response.

ADMINISTRATIVE DATA

Inspected firm:	Novartis Consumer Health
Location:	10401 Hwy 6 Lincoln, NE 68517-9626
Phone:	402-464-6311
FAX:	
Mailing address:	10401 Hwy 6 Box 83288 Lincoln, NE 68517
Dates of inspection:	6/13/2011, 6/14/2011, 6/15/2011, 6/17/2011, 6/20/2011, 6/21/2011, 6/22/2011, 6/23/2011, 6/27/2011, 6/29/2011, 7/1/2011, 7/8/2011
Days in the facility:	12
Participants:	Eric M. Mueller, Investigator Joseph R. Lambert, Investigator

(Written by EMM)

On 6/13/11, I arrived to Novartis and requested to speak to the most responsible person. I was introduced to Mr. Terence J. Walsh, Site Leader. At this time, I showed credentials to Mr. Walsh and issued an FDA 482, Notice of Inspection. I also told him the purpose of the inspection was to review solid dosage form mix-ups reported via consumer complaints and continuing 3-day Field Alerts.

On 6/20/11, Investigator Joe Lambert joined the inspection to provide assistance and collect documentary samples. We showed credentials to Mr. Walsh and issued an FDA 482, Notice of Inspection.

On 7/8/11, we issued a 13-item to Mr. Terence J. Walsh, Site Leader.

All photos exhibited in this report were taken with the firm's camera and printed at their facility. No pictures were taken with an FDA issued camera, per the firm's request.

HISTORY

(Written by JRL)

Novartis Consumer Health, Inc. (NCH) was incorporated in Delaware 12/20/94. They continue to manufacture non-sterile human and animal pharmaceuticals distributed throughout the US and internationally. NCH was incorporated into the state of Nebraska on 12/23/1996. This location manufactures human solid dosage form products, human liquids, human creams, human suspensions, and human powder products. The location also manufacturers animal solid dosage forms and suspensions.

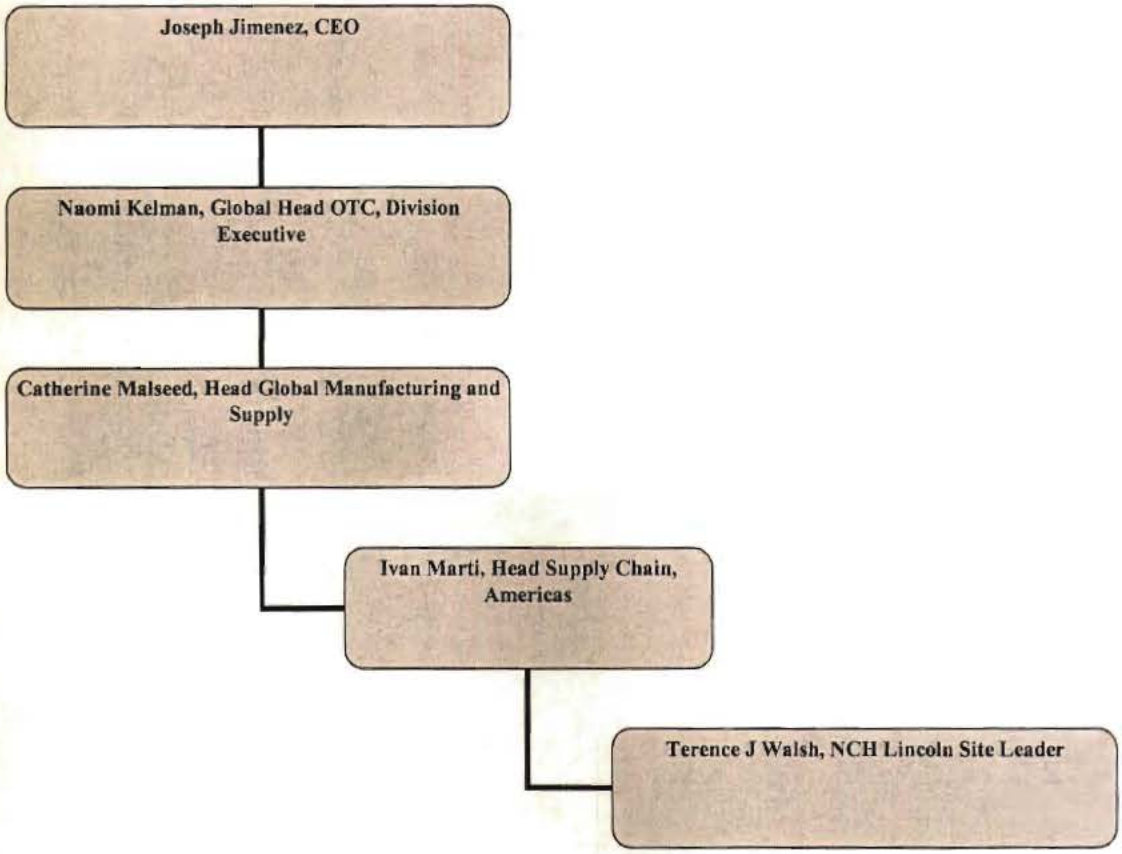
The plant at 10401 Highway 6, Lincoln, NE is over (b) (4) square feet and sits on approximately (b) (4) acres of land. The facility produces approximately (b) (4) units per year under 43 brands, 170 formulations, and [redacted] SKU's (Stock-keeping units). The facility exports products to (b) (4) countries. The facility has the manufacturing capability for the following profiles: tablets (bi-layer, press coated, caplets, wax matrix), liquids (solutions, suspensions, syrups), creams/ointments, hard gelatin capsules, patch technology, and high-potent compounds. The facility also has the packaging configuration capability for blisters (film/foil, foil/foil), bottle (liquids, tablets, capsules, and granules), manual assembly (displays, promotional packs), tubes (metal, plastic), pouches, and patches (not as a drug delivery device).

The functions which are represented on the Lincoln site range from innovation to supply. These functions include R&D, Quality, Supply Chain, Finance, Human Resources, Production, Engineering, and Customer Service. The number of employees at the facility ranges from (b) (4) associates. These associates include (b) (4) from production, (b) (4) from quality, (b) (4) from engineering, and (b) (4) R&D employees.

Mr. Joseph Jiminez is the Chief Executive Officer (CEO) of the Novartis Group located at the World Corporate Headquarters in Basel, Switzerland. There are currently seven divisions (each division being an individual legal entity) under the Novartis Group. These divisions are as follows: Consumer Health, Ciba Vision, Animal Health, Pharma, Vaccines and Diagnostics, and Sandoz. Each division has its own CEO who reports directly to Mr. Jiminez.

Ms. Naomi Kelman is the Global Head OTC, Division Executive/CEO, which oversees the operations at this facility. Ms. Kelman is located at NCH Corporate Headquarters, 200 Kimball Dr., Parsippany, NJ 07054-0622. Copies of organizational charts (from management at the Lincoln site reporting to Ms. Kelman to the ultimate authority, Mr. Jiminez) are attached under **Exhibit JRL 1.** Mr. Terence J Walsh, Site Leader, is the most responsible person at the Lincoln Novartis facility and he reports to Ivan Marti, VP Supply Chain America in Parsippany, NJ. Ivan Marti reports to Catherine Malseed, Head Global Manufacturing and Supply, whom reports to Naomi Kelman, Global Head OTC.

Organizational Chart from Joseph Jimenez, CEO to Terence Walsh, Site Leader



The firm has two off site warehouses for temporary storage. Both are located less than 4 miles from the firm. No controlled substances are housed at either warehouse. All controlled substances are stored at the main facility. The following details a description of products stored at the two warehouse facilities.

- **FEI: 3004311599, Novartis Consumer Health, Inc. "Fletcher Warehouse", 6500 Fletcher Avenue, Lincoln, NE 68507,** finished product storage, raw material storage, and some packaging material storage are located at this site.
- **FEI:** (b) (4) (b) (4) is a public storage warehouse, not operated by Novartis. This site is used to warehouse retain samples, packaging materials, and equipment. No finished product is stored at this facility.

There are (b) (4) production shifts: (b) (4) (b) (4) The laboratory employees work (b) (4) shifts which mirror the (b) (4) production shifts. The microbiology laboratory has (b) (4) shift with coverage from (b) (4)
The office hours of management are 9:00 a.m. to 5:00 p.m. Monday through Friday.

FMD-145 letter should be sent to the following:

Terence J. Walsh, Site Leader
10401 Highway 6
Lincoln, NE 68517-9626

Additional correspondence should be addressed to:
Naomi Kelman, Global Head OTC, Division Executive/CEO
200 Kimball Dr
Parsippany, NJ 07054-0622

I reviewed the firm's response to the previous FDA 483, Inspectional Observations, issued on 4/16/10. There were two observations during the previous inspection. I confirmed corrections had been implemented which were detailed in their response. I had no objections to the firm's response to these items. A copy of the firm's response can be viewed at **Exhibit JRL 2**.

INTERSTATE COMMERCE/JURISDICTION
(Written by JRL)

Please refer to **Exhibits JRL 3, 4, & 5** for master listings of all products manufactured by this NCH-Lincoln facility. These 3 categories are as follows: (b) (4) and Animal Health Products (**Exhibit JRL 3,** Animal Health Products begin on page 5), Solid Products (**Exhibit JRL** 4), and Liquid and Cream Products (**Exhibit JRL 5**). The firm contract manufacturers for companies listed on **Exhibit JRL 6**.

Finished products are delivered via company vehicle from the Novartis manufacturing facility to the (b) (4) warehouse. The firm ships (b) (4)% of the products they manufacture out of the State of Nebraska. The following three locations are distribution centers, in which Novartis delivers finished product:

- (b) (4) -Animal health products, third party contract products, and products for markets outside the US
- (b) (4) NCH Human OTC drug products
- (b) (4) manufactured products and animal health

Representative labels of (b) (4)% of Novartis Consumer Health products can be viewed at **Exhibit JRL 18**.

TRAINING

(Written by JRL)

I reviewed procedure QAP-034-09, "Site Training Policy", effective (b) (4). The purpose of this document is to ensure all site associates and contractors are properly trained to perform requiste job duties in a GMP environment. The document also defines the site and department specific training program structure. The firm currently has all new employees perform Good Manufacturing Practice (GMP) training. The firm also requires all employees to accomplish annual GMP training.

I reviewed the training records of the following Quality Assurance employees: (b) (6) (b) (6), (b) (6), (b) (6), (b) (6), (b) (6), (b) (6) and (b) (6) (b) (6). I was provided by the firm a list of procedures in which each of these employees had been trained. I focused my review of these trainings to the complaint procedure. I confirmed all seven of these Quality Assurance employees had completed the training for SOP "Complaint Handling Procedure", version 4. The training for this procedure was completed during the last quarter of 2010.

See Observation 12 in the "Objectionable Conditions and Management's Response" section of this report for deficiencies in training, with emphasis on the complaint handling process training.

INDIVIDUAL RESPONSIBILITY AND PERSONS INTERVIEWED

(Written by EMM and JRL)

Terence J. Walsh, Site Leader:

Mr. Walsh has been in this position for roughly b(6) years. Prior to this position he worked at a different pharmaceutical company in (b) (6) as a Director of Operational Excellence. He has a mechanical engineering degree from (b) (6). He identified himself as the most responsible person at the firm. He said he is responsible for the operations at Novartis Consumer Health Lincoln (referred to as NCH-Lincoln in this report). He is also responsible for engineering on site, supply chain management and logistics. He reports to Mr. Ivan Marti, VP Supply Chain America in Parsippany, NJ.

Polly Harris, Director of Quality Assurance (QA) and Compliance:

Ms. Harris has worked at this facility for roughly b(6) years. She has been in this position for b(6) years and reports to Mr. Joseph Delaney, Head of QA and Compliance OTC Americas. She was available throughout the inspection assisting with answering most of our questions and providing records we requested.

Joseph Delaney, Head of QA and Compliance OTC Americas:

Mr. Delaney has been in this position for roughly (b) (6) year. His previous position was Head of QA OTC North Americas. He has been working at Novartis for approximately (b) (6) years. He was available throughout this inspection providing answers to many questions. He reports to Ms. Jila Breeze, Global Head of OTC Quality.

Vivianne Arencibia, Vice President QA:

Ms. Arencibia joined the inspection from corporate headquarters on 6/20/11. She has been with Novartis since b(6) and works as the Head of Compliance and Auditing world-wide. She told me she joined the inspection to support key inspections and evaluate the overall inspection process. She reports to Juan Andres, Global Head of Novartis Group Quality.

(b) (6), **Process Engineer**, is responsible for overseeing quality on the (b) (4) packaging line and any product which is packaged on this line. He provided information pertaining to the cleaning validation. His supervisor is Sree Vadlamudi, Engineer Lead.

(b) (6), **QA Anaylist II**, is responsible for batch review and investigation review. She provided information regarding batch records. She reports to Heidi Brokennicki.

(b) (6), **Contract Supply Facilitator**, is responsible for overseeing the packaging line for contract supply products. He provided information during the tour on the line (b) (4) packaging line.

(b) (6) **Quality Engineering**, is responsible for reviewing documents for equipment related validations of processes. He provided information on process sampling. He reports to Chris Scott, Quality Engineering Supervisor.

(b) (6), **QA Analyst II**, is responsible for overseeing the Quality review of the contract supply chain. He provided information on sampling plan.

(b) (6), **Process Technician**, is responsible for operations on the (b) (4) packaging line. He provided information on packaging process sampling. He reports to b(6) Contract Supply Facilitator.

(b) (6), **Analyst I**, is responsible for Quality Assurance label review for incoming labels and labels issued to the packaging lines.

(b) (6), **Process Engineer,** is responsible for overseeing the process engineering of the liquid dosage form packaging operations. He provided information pertaining to cleaning validation.

(b) (6), **Facilitator Manager**, is responsible for overseeing the operations on packaging lines (b) (4) and (b) (4)

PENDING ISSUES:
(Written by EMM)

The below chart is a summary of Field Alerts I covered during this inspection and a brief description of the result after FDA review.

Field Alerts Covered:

Date:	Filed By:	Product	Reason	Result of FDA Inspection
(b) (4)	(b) (4) (b) (4)	(b) (4) Lot: (b) (4) (b) (4)	(b) (4) (b) (4) mixed with (b) (4) (b) (4)	(b) (4) **voluntarily recalled this product. Please refer to Exhibit EMM 1 for details.**
(b) (4)	(b) (4) (b) (4)	(b) (4) (b) (4) Lot: (b) (4)	Plastic tape found in a bottle	No deviations noted upon review.
(b) (4)	(b) (4) (b) (4)	(b) (4) (b) (4) lot: (b) (4)	Product mix-up	(b) (4) **voluntarily recalled this product.**
2/22/11	Novartis	Excedrin Migraine Caplets Lot: 10101757	Wrong product in bottle	Please refer to Observation 8-C for details.
2/8/11	Novartis	Excedrin Migraine	Product mix-up	Please refer to Observation 4-C for details.

		10039449		
	(b) (4) (b) (4)	(b) (4) mg tablets	Dissolution	No deviations noted upon review.
10/15/10	Novartis	Excedrin Migraine, Lot: 10087498	Product mix-up	Please refer to Observation 3-A for details.
7/9/10	Novartis	Excedrin Migraine, Lot: 10087500	Foreign Object in bottle	No deviations noted upon review.
(b) (4)	(b) (4) (b) (4)	(b) (4) (b) (4) mg lot: (b) (4)	Product mix-up	(b) (4) **voluntarily recalled this product.**
4/2/09	Novartis	Excedrin Migraine Caplets lot: 10043250	Product mix-up	Covered during previous inspection 4/10.
2/17/09	Novartis	Excedrin Migraine lot: 10058605	Product mix-up	Covered during previous inspection 4/10.

FACTS COMPLAINT: 11599. (Prevacid 15 mg) See Observation 8-A for details of problems with the firm's handling of this complaint.

FACTS COMPLAINT: 65559. This complaint was covered during an inspection 4/09 at this facility.

Please refer to Exhibit EMM 2-4. These are field alerts filed 6/29/11 as a result of this inspection. An initial review of these Field Alerts revealed similar problems as those described in Observations 1-13 below.

MANUFACTURING/DESIGN OPERATIONS
(Written by JRL)

Packaging Process

The firm's main packaging lines are lines (b) (4) and (b) (4). All Excedrin products are packaged on lines (b) (4) and (b) (4) (See **Exhibit JRL 4**), while all (b) (4) products (See **Exhibit JRL 3**) are packaged on line (b) (4). An overhead view of packaging line (b) (4) can be viewed at **Exhibit JRL 7**. All b(4) of the mentioned packaging lines are similar in equipment (See list of equipment **Exhibit JRL 8**) and have similar floor plans. The packaging process and flow is also similar on all b(4) lines.

b(4)

(b) (4)

(b) (4)

Equipment (Packaging Line Validation)

I reviewed document 06-664-COM, "(b) (4) Commissioning (b) (4) bottle packaging line", approved 1/5/07. The purpose of this document is to provide verification the bottle packaging line in room (b) (4) is installed and operates correctly. It also documents all direct quality impact components are capable of consistently packaging within pre-determined limits and tolerances.

This commissioning involved a verification of each piece of equipment to ensure it was installed correctly. This was performed by a visual verification. The equipment examined included the following: bottle unscrambler, desiccant feeder, tablet filler, (b) (4) metal detector, capper, sealer, labeler, cartoner, sealer, printer, conveyer, and barcode reader. The commissioning included a functional testing of the packaging line at multiple speeds with varies bottles.

The commissioning included a verification of filling for bottles sized at 30 cc and 400 cc. Each of these bottles was tested at a minimum speed of (b) (4) bottles per minute and maximum speed of (b) (4) and (b) (4) bottles per minute, respectively. The commissioning was successful and supported ability of the firm to package products on this line. I asked Polly Harris, QA, if there was an evaluation on the ability of an employee to consistently detect a foreign tablet at various filling speeds. She informed me the firm has not performed an evaluation of an employee's ability to detect foreign tablets at various filling speeds.

During my tour of packaging lines (b) (4) and (b) (4), on 6/23/11, the speed of the filler were (b) (4) bottles per minute for (b) (4) count bottle and (b) (4) bottles per minute for an (b) (4) count bottle, respectively. The speed of packaging line (b) (4) appeared to be quick and I witnessed the operator stopping the filler (b) (4) or (b) (4) times during my (b) (4) minute observation period. These stoppages were due to missing tablets in the slats, which are filled by the filler operator. The speed of packaging line (b) (4) was slower and I did not witness any operator stoppages.

I reviewed document (b) (4) Bottle Packaging Line (b) (4) Performance Qualification Report", approved by Quality on 2/8/08. This qualification report was similar to the (b) (4) Packaging line, which was reviewed above. The results of the qualification were the packaging line has the ability to consistently package bottles in a range of (b) (4) to (b) (4) count bottles.

I also reviewed document number 07-014-IOPQR, "(b) (4) Bottle Packaging Line (b) (4) Equipment Installation, Operational, and Performance Qualification, Final Report", approved by the Quality Department on 2/14/07. The purpose is to document the satisfactory installation, operation, and performance of the Bottle Packaging Line (b) (4). The performance qualification was successful with no deviations.

See Observation 5 in the "Objectionable Conditions and Management's Response" section of this report for deficiencies in equipment identification.

Packaging Line Sampling

I reviewed document QAP-0440-04, "Process Monitoring", effective 6/14/10. The purpose of this document is to provide the instructions and guidelines used to monitor the manufacturing processes located throughout the Lincoln facility. This procedure serves as a reference document to delineate the general criteria used to conduct the process monitoring activities consisting of the collection of process variables and attribute data. The document details the sampling plan and action, control, and reasonable limits of packaging and labeling activities.

This procedure establishes in-process sampling based upon reliability of the process. The general status criteria are established under three process criteria: Unproven/New process, established process, and robust/proven process. Each of these three criteria have established sampling sizes per (b) (4) units and control limits, which coincide with each sampling size. This procedure also states the following: "There may be instances or conditions where a more stringent sampling frequency is warranted". Polly Harris, QA informed me there are no guidelines or definitions of these "instances or conditions" where more stringent sampling frequency is warranted. These instances are driven by investigations or when deemed warranted. She also informed me the sampling frequency of packaging lines (b) (4) and (b) (4) had not changed in the past 3 years.

The current sampling plan for packaging lines (b) (4) and (b) (4) include a sampling of the first (b) (4) bottles filled on the packaging line. Each of these (b) (4) bottles is removed and the product inside the bottle is counted for filling accuracy. If no discrepancies are discovered in these (b) (4) bottles, then the packaging process begins. The sampling rate for all Excedrin products was (b) (4) bottle for every (b) (4) bottles produced. The sampled bottle is opened and the solid dosage form product inside the bottle is examined for foreign product, visual defects, and filling accuracy.

I asked Polly Harris, QA, if she felt the sampling plan was appropriate based upon the complaints and investigations pertaining to mix-ups. She informed me the sampling plan is appropriate.

Packaging Line Cleaning Validation

I reviewed SOP FAD-295-08, "Equipment Use and Cleaning Procedure", effective 12/28/10. The purpose of this document is to outline allowable hold times and campaign length for manufacturing and packaging equipment during processing, cleaning, and storage. This procedure is considered a universal cleaning procedure for all cleaning activities at NCH. The procedure defines a campaign as a series of batches of products that can be produced without a major clean. It also establishes (b) (4) batches as the maximum number of identical product batch campaigns before a major clean is necessary. The procedure requires a minor clean in between each batch of product.

The procedure also described the use of clean tags to identify the status of equipment which has been cleaned following use in manufacturing and packaging of drug product. It also describes the methods of protecting cleaned equipment prior to production usage and equipment requirements for transporting portable equipment. The procedure also covers actions to be taken when a foreign contaminant/material is found on product contact surfaces during manufacturing or packaging. If foreign material or contaminate are found, production staff must immediately contact the Quality Department.

I also reviewed the minor/major clean grid. This grid indicates when a major or minor clean must be performed based on product. There were (b) (4) separate grids which covered cleaning for bin blenders, compression equipment, and (b) (4) Packaging equipment.

I was informed by (b) (6) Process Engineer, the process of performing a major clean a packaging line takes on average (b) (4) He informed me the speed of the cleaning process is not dependent on the number of people cleaning. This is because each step must be performed before the next step can begin and most of the steps involve disassembling equipment. This appeared to be true during my review of the above batch records in which major cleans were taking approximately (b) (4) (b) (4) to perform.

The firm documents cleaning in the packaging area in a log identified as a "sequence log". This log documents the sequence of products which were packaged on a particular packaging line. It also

documents the level of clean performed (major or minor) between two separate batches. In addition to the sequence log, the firm documents in each batch record the steps performed during the clean (batch record document has much more detail). I reviewed the following batch records to verify cleanings between batches (these batches were identified in complaints as having NCH/NCH product mix-ups):

Lot Number	Product	Prior Product	Prior Level of Clean
10099302	Excedrin ES Caplet	Excedrin Express Gels	(b) (4)
10078599	Excedrin AFTH Express Gels	Excedrin Back and Body Caplets	(b) (4)
(b) (4)	(b) (4) mg	(b) (4) mg	(b) (4)
(b) (4)	(b) (4) mg	(b) (4) mg	(b) (4)
10101757	Excedrin Migraine Caplets	Excedrin Caplet 24	(b) (4)
10100866	Excedrin ES Tablet	Excedrin Migraine	(b) (4)
10099327	Excedrin Extra Strength	Excedrin TH Caplet	(b) (4)
10092774	Excedrin TH Caplet	Excedrin TH Caplet	(b) (4)
10096739	Excedrin PM Tablet	Excedrin PM Tablet	(b) (4)
10096735	Excedrin PM Tablet	Excedrin ES Capsule	(b) (4)
10099300	Excedrin ES Tablet	Excedrin MC Express Gelcaps	(b) (4)
10107936	Excedrin Migraine Geltab	Excedrin Migraine Geltab	(b) (4)
10082668	Excedrin ES Express Gelcap	Excedrin ES tablet	(b) (4)

The firm bases all of their cleaning procedures off of the original validation 04-014, "(b) (4) Packaging Line Procedure Cleaning Procedur (b) (4) ", completed 6/7/04. This validation was performed to demonstrate the effectiveness of the cleaning procedure (b) (4) used to clean the (b) (4) packaging line (b) (4) filler. This validations main focus was on microbial and residue cleaning, not tablet/caplet clearing. No deviations were noted.

(b) (4) consecutive repetitions with acceptable results were completed for active residues. The firm performed (b) (4) episodes following cleaning of the equipment after b(4) packaging (most water insoluble packaged product at the firm) were completed, as well as (b) (4) following cleaning of the equipment after (b) (4) packaging. These two products were b(4) due to their active ingredient's insolubility in water and similarities in cleanability. This validation concluded that the

procedure is adequate for the cleaning of residues and microbiological growth on the packaging lines. This validation applied to the cleaning of the following equipment in the packaging line: bottle unscrambler, desiccant feeder, (b) (4) filler/filler parts, metal detector, capper, induction sealer, cap tightner, labeler, cartoner, bundler, and miscellaneous equipment.

The firm then performed cleaning validation assessments on all other packaging lines. These assessments evaluated the worst case product, batch size, and filler equipment. I reviewed the following two cleaning validation assessments, which are all based off of validation (b) (4) (b) (4) Packaging Line Filler (introduction of new products) and (b) (4) Packaging Line Fillers (replacement of the fillers in the work center).

The cleaning procedures used in the above validations were reviewed. I reviewed SOP (b) (4) (b) (4) Line Work Center Cleaning Procedure", effective 1/25/08, and SOP (b) (4) Line Work Center Cleaning Procedure", effective 1/25/08. The purpose of these procedures is to describe the major and minor cleaning processes for the (b) (4) and (b) (4) packaging areas. These procedures detail each step for cleaning each piece of equipment in the packaging line. The primary difference between these two procedures is the room location in which each procedure is performed.

It is important to note, prior to this inspection this procedure required an authorized factory representative is to inspect all parts that have been disassembled and cleaned before storing or reassembling parts. The firm has adjusted this procedure and now requires a Quality representative to verify the disassembly and cleaning before storing or reassembling parts. I verified this procedural change through a review of a planned deviation 92712 (**Exhibit JRL 16**), which applies to packaging lines (b) (4) and (b) (4)

I reviewed changes to the cleaning procedure for work centers (b) (4) and (b) (4). The following items were documented on change control documents:

1/29/08 – A (b) (4) step was added after the last (b) (4) and before the use of (b) (4)

4/28/08 – The procedure was updated to provide clarification to reduce the number of operators working with rejected bottles on the packaging line.

6/4/08 – Transfer of (b) (4) and (b) (4) into work centers (b) (4) and (b) (4)

11/12/08 – Added (b) (4) in the (b) (4) line.

2/5/09 – New equipment update which included the (b) (4) and (b) (4).

1/23/09 – Clarity for cleaning and inspection for major cleans

9/1/09 – The removal of (b) (4) from the cleaning record and now only use the terms major and minor clean. This decreased the probability of cleaning errors.

I toured packaging room (b) (4), on 6/23/11, in which Excedrin Migraine Caplets, 100 ct bottles, Lot 10116782, were being packaged. The room appeared to be clean with one employee in the room actively monitoring the (b) (4) tablet filler (**Exhibit JRL 9, page 4**). The filler was running at (b) (4) bottles per minute, which kept the employee actively monitoring the slats. The employee monitoring the filler stopped the filler (b) (4) to (b) (4) times during the 10 minutes I was in the room. These periodic pauses were necessary to fill an empty slat hole.

I then toured packaging room (b) (4) on 6/23/11, in which Excedrin Migraine Caplet, 8 ct bottles, Lot 10116779. The room appeared to be clean with one employee in the room actively monitoring the (b) (4) tablet filler (**Exhibit JRL 9, page 9**). This filler was running at (b) (4) bottles per minute, which was much slower than the previous room. This was due to fewer tablets going into smaller bottles.

Neither of these rooms (b) (4) had controlled access to them. The filling lines in both of these rooms were managed by one employee with no other employees in the room (See **Exhibit JRL 9, page 4 & 9** for photo). I inspected the employees' uniform in both rooms. Both of these employees were in white company issued uniforms (See **Exhibit JRL 9, page 4 & 9** for photo of uniform). The uniforms did not contain any pockets or areas where foreign contaminates could be concealed. However, with little oversight in the room, it would appear the potential for intentional contamination is possible.

I toured packaging line (b) (4), on 6/23/11, in which (b) (4) mg tablets, lot (b) (4). This line was access controlled due to the packaging of controlled drug substances. This line was monitored with video surveillance. The video surveillance was used to monitor employee activity such as cleaning, packaging, or filling. The line also had multiple employees working on the packaging area. A photo of the line can be viewed at **Exhibit JRL 9, page 10**.

See Observation 13 in the "Objectionable Conditions and Management's Response" section of this report for deficiencies in cleaning documentation.

Raw Material (Incoming label review)

On 6/30/11, I toured the incoming label review operations. Labels are given a unique material number when the labels are received from the vender. The Quality Assurance Label team then receives notification to review the incoming label. They begin the review by identifying the incoming label's specification sheet, which is located in a computer database with "view" rights only. This database holds the original proofs (which have been verified and signed off by the

Quality team) of all the incoming labels. b(4)
b(4)

b(4) Once all of the parameters of the label are reviewed, the Quality Assurance Label team approves the label in the (b) (4). The label and its approved parameters are then reviewed by a second Quality Assurance person before the labels can be used in packaging. Once both reviews are complete, a certificate of analysis is generated for the labels.

I also toured the label storage area. Labels are stored in a controlled access area (as are the activities described above). The Quality staff which accompanied me to the label area did not have keys and were required to ring a bell to entire this area. Once in the label area, (b) (6), Warehouse Specialist, demonstrated the process of obtaining labels from the warehouse and issuing them to packaging staff.

Labels inventoried before they exit the controlled label storage area. They are then taken to a "staging" area where all packaging components are gathered and organized. At the beginning of packaging, these components are all inventoried. After packaging has been completed, access labels are returned to the label storage area for reconciliation.

I reviewed the following procedures which pertained to label acceptance and issuance:

SOP QID-005-00, "(b) (4) Robotic Artwork Proof-Reader" effective 10/17/07. The purpose of this is to provide general instructions to operate the (b) (4) b(4) Artwork Proof-Reader.

SOP QAD-021-05, "Quality Assurance Disposition of b(4) Materials", effective 2/26/10. The purpose of this procedure is to describe the Quality Assurance disposition process for b(4) raw and packaging material.

SOP FPD-014-05, "Packaging Supplies Verification", effective 2/16/10. The purpose of this procedure is to describe the activities necessary to verify the packaging supplies prior to use on a packaging work center.

SOP QID-002-04, "Checking and Approval of Packaging Supplies", effective 4/29/08. The purpose of this procedure is to describe the process of testing, checking, and approving packaging supplies, and documentation requirements in Quality Assurance.

MANUFACTURING CODES
(Written by JRL)

Novartis Consumer Health utilizes an 8 number lot code for a majority of their finished products. This code is randomly assigned by their (b) (4) inventory control system. The (b) (4) assigns a (b) (4) batch number for all materials. This number is 8 characters long with a number range between (b) (4) to (b) (4) The following are variations to this 8 character number system.

(b) (4)
An (b) (4) suffix precedes a (b) (4) assigned sequential batch number. Example (b) (4)

Animal Health Products:
These products contain an 8 character numeric lot number assigned by the (b) (4)

Pedinol (Gris-Peg):
This product contains an 8 character numeric lot number assigned by the (b) (4)

Purchased Goods (Raw materials, package supplies):
These products are given an 8 character numeric lot number assigned by the (b) (4)

COMPLAINTS
(Written by JRL)

The complaint process begins at a call center. The call center is contracted by NCH to handle the communication with customers for complaints (most recently (b) (4) since August (b) (4), prior to that (b) (4)). Employees at the call center obtain the initial information from the complainant and input this information into an electronic database. If the complaint is for a "foreign" tablet or object, the call center employee sends a postage paid return package to the complainant. Once the call center employee completes the initial interaction with the complainant, the complaint is sent to NCH for review by a Complaint Manager at the NCH Quality Department. A flow chart of the above process can be viewed at **Exhibit JRL 10, page 2**.

The Complaint Manager receives the initial complaint from the call center and reviews the complaint. It is the Complaint Manager's responsibility to investigate the complaint and close these complaints. The Complaint Manager deems the complaint as critical, major, or minor. The critical complaints are investigated more thoroughly than the major and minor complaints. The more thorough review includes a review of manufacturing documents during the investigation. The

Complaint Manager then performs a complaint lot trend and reports any trend to NCH Quality Management. A flow chart of the above process can be viewed at **Exhibit JRL 10, page 1**.

See Observations 2, 3, 6, 7, 9, 10, and 11 in the "Objectionable Conditions and Management's Response" section of this report for deficiencies regarding complaint handling.

RECALL PROCEDURES
(Written by JRL)

Investigator Lambert reviewed SOP 202405, "Product Recall Assessment for NCH OTC", effective 1/31/09. The purpose of this procedure is to detail both the responsibilities and requirements from the organization to promptly and effectively recall products from the market. The procedure can be viewed at **Exhibit JRL 11**. No deviations were noted.

OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE

Observations listed on form FDA 483

OBSERVATION 1

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

Specifically,

Your Quality Unit has failed in the responsibility and authority to monitor Quality Systems designed to assure the quality of drug products manufactured and packaged at your firm. This failure is evidenced in the Observations below (2-13), as well as continued NDA Field Alerts and recalls for similar problems over the last several years.

Discussion with Management:
(Written by EMM)

This inspection revealed numerous deficiencies in the firm's Quality Unit oversight of products manufactured and packaged at this site.

I asked Mr. Delaney on 6/15/11 why these deficiencies (see Observations and explanations below) were not recognized internally by Novartis? He told me "I need to investigate why these issues were not recognized."

I asked Ms. Harris about the problems and she said "we agree we have deficiencies and will go back and do what we said. We are going to make the investigations correct. We have work to do as we are going to open each complaint."

Please refer to Exhibit EMM 5. This letter, dated 6/21/11, was given to me as a formalized corrective action summary. This summary was written during this inspection and is intended to address concerns raised by this FDA inspection as well as concerns identified in an internal audit (May 2011).

I asked Ms. Harris about the Observations identified during this inspection and she said "There has been complacency in the way we've always done things. We didn't step up and change complaint procedures when we ought to." She also told me "this is the way we've been addressing investigations for years."

OBSERVATION 2

Written records are not always made of investigations into unexplained discrepancies and the failure of a batch or any of its components to meet specifications.

Specifically,

You have failed to open deviation investigations into numerous "critical" consumer complaints of foreign products found inside the drug products manufactured at your firm.

Specifically,

In the year 2010, you had 26 complaints where solid dosage form products (with confirmed mix-up complaints of Novartis Consumer Health "NCH"-Lincoln manufactured product) were returned to your site, by a customer, and no official investigation was opened.

In the year 2009, you had 13 complaints where solid dosage form products (with confirmed mix-up complaints of NCH-Lincoln manufactured product) were returned, by a customer, to your site and no official investigation was opened.

This is important because a total of 40 confirmed returned consumer complaint samples (containing mix-ups of NCH-Lincoln manufactured solid oral dosage form products) have not been adequately investigated by your firm.

Additionally,

You have failed to adequately investigate 166 complaint instances of foreign tablets in your drug products since 2009.

These instances refer to examples where the suspected solid dosage oral products were not returned by the complainant to the firm and no follow up was conducted by your Quality Unit.

Lastly,

Your Quality Unit's neglect to follow up with the complaint is a failure to follow Procedure SOP-202891, Conducting Deviation Investigations.

Discussion with Management:
(Written by EMM)

Exhibit EMM 6 shows a summary of foreign product returned complaint samples for 2010.

Exhibit EMM 7 shows a summary of foreign product returned complaint samples for 2009.

In 2010, there were 26 CRITICAL complaint instances where NCL-Lincoln manufactured product mix-up complaint samples were returned to the site. In these instances, no official (b) (4) investigation was opened into the problems identified by the complainant and the returned samples. (see blue highlight dots in Exhibit EMM 6)

In 2009, there were 13 CRITICAL complaint instances where NCL-Lincoln manufactured product mix-up complaint samples were returned to the site. In these instances, no official (b) (4) investigation was opened into the problems identified by the complainant and the returned samples. (see yellow highlight in Exhibit EMM 7)

The above indicate a pattern of problem where the firm receives confirmed information about a similar problem, but does not open official (b) (4) investigations into the matter, despite procedures obligating them to do so.

Please refer to Exhibit EMM 8 for a copy of the firm's "Conducting Deviations Investigations", procedure SOP-202891, dated 6/30/10. This procedure, in part, describes a deviation event as "Product defects (reported from internal and external sources)". The above instances where product was returned to the firm and confirmed to contain different products of NCH-Lincoln produced products fit this description and the procedure of conducting deviation investigations should be applied.

The procedure on page 4 describes the Quality Assurance responsibilities that were not followed in the above instances.

I asked Ms. Harris why there are no (b) (4) investigations for the above returned and confirmed instances of NCH-Lincoln produced products. She told me, "we did not notice this as a problem until this weekend" (6/18/11).

It is important to understand that because of the firm's failure to open and thoroughly conduct adequate investigations into the continued problem of NCH-Lincoln produced drug products (as well as the observations shown below), there is no way of determining how widespread the mix-up problem is at this firm.

Mr. Walsh, Ms. Arencibia and Ms. Harris told me they agreed with my statement of not being able to assess how widespread the mix-up problem is at this firm.

Ms. Arencibia told us on 6/20/11 "We have not done a good enough job of ruling out the possibilities that this is not happening." This was in reference to the firm's consistent investigation conclusions stating, in part, product mix-ups "occurred outside of Novartis control".

Unreturned Packages:

It is important to understand that when a complainant calls in a critical complaint, Novartis is procedurally obligated to mail postage paid mailing materials for the customer to return the suspect product. (See Observation 10-B for further details).

Please refer to Exhibit EMM 9. This shows a list of foreign product complaints where packages were sent to customers for the years 2009-2011. The entire list contains 166 instances in the past 3 years where packages were sent to customers, but never returned.

When packages do not arrive back (see the 166 instances), NCH-Lincoln will close (b) (4) reports and state "package not returned". No further follow up is conducted by NCL-Lincoln despite known problems into mix-ups.

I asked Ms. Harris why this facility does not investigate further about these types of complaints and she said "we don't have procedures requiring it."

I explained to management that this firm has a known history of mix-up problems. Additionally, knowing this fact, sending out a package with no further follow up (see 166 instances above) is inadequate.

Mr. Delaney told me "we will go forward and do whatever we can. If we don't get them back (packages), we will contact the customers directly." He also said, "Right now, the investigation ends once a package is not returned."

Mr. Delaney and Ms. Harris told me they understood my concerns and realize they should do more with investigations into critical complaints. Mr. Delaney told me "all of these complaints will be re-evaluated." I recommended they use a risk-based approach to their proposal to re-review their complaints. Specifically, I was referring to product that was on the market. They told me they understood. Please refer to Exhibit EMM 5 for details on how they propose to address the issues identified during this inspection.

I requested several times a list of product and where they are packaged in the firm. This list took several days and multiple requests before it was provided to me. Please refer to Exhibit EMM 10. This list shows a listing of products that are produced on packaging lines (b) (4) and (b) (4). **These two packaging lines are where a majority of the mix-up complaints are packaged. It is important to understand these are non-dedicated packaging lines where a lot of different products are packaged.**

Exhibit EMM 11 shows a listing of controlled substances packaged on non-dedicated line (b) (4). This line is used for packaging the (b) (4) products subject to recent recalls (by (b) (4) (b) (4).

OBSERVATION 3

Investigations of an unexplained discrepancy 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.

Specifically,

You have failed to extend investigations to all batches of product potentially affected by a problem.

For example,

A) Your Quality Unit failed to extend the investigation to all lots/batches of product potentially affected for a recent mix-up complaint of Excedrin Migraine Tablets, Lot # 10087498, mixed with Excedrin Migraine Caplets. This complaint is associated with NDA Field Alert, dated 10/15/10.

Lastly, the conclusion of this investigation, reads in part, "it is not possible that the products were mixed within Novartis control." does not appear to be supported by the evidence in your investigation. The two products in the complaint sample were actually packaged on the same equipment within 4 orders of each other. Also, the investigation revealed several areas in the process where the two products could have possibly come into contact (compression, film coating, transport, packaging).

B) Your investigation of Unplanned Deviation PR, No: 88510, (opened March 2, 2011) investigating complaint 10656633 of mixed Excedrin Extra Strength caplets, Lot: 10099302 with Excedrin ES Gelcaps did not extend to all lots/batches of product potentially affected. In this instance, the two products were packaged on the same line b(4) consecutively.

These are just two examples of numerous instances in which your firm's deviation investigations do not extend to other lots/batches of product potentially affected by the problem.

THIS IS A REPEAT DEFICIENCY FROM THE PREVIOUS INSPECTION AT YOUR SITE, DATED 4/5-16/10.

Discussion with Management:

(Written by EMM)

Please refer to Exhibit EMM 12 for a copy of the firm's complaint investigation report, NDA Field Alert, and unplanned deviation report into a recent mix-up complaint of Excedrin Migraine Tablets, Lot # 10087498, mixed with Excedrin Migraine caplets.

The investigation into this complaint concluded, in part, "based on this investigation it is not possible that the products were mixed within Novartis control."

The evidence in the investigation shows that the two products in the complaint sample were packaged on the same equipment within 4 orders of each other. Also, the investigation revealed several areas in the process where the caplets could possibly have come into contact (compression, film coating, transport, packaging).

Because the firm feels there is not possible for this type of mix-up to occur within their control, they did not extend the investigation to other lots.

I told them based on my assessment, their conclusion is incorrect. I also told them I felt that the probability of a mix-up on non-dedicated packaging equipment occurring within four orders of each other greatly increases the possibility of the mix-up occurring within their control.

Management told me they understood my concerns and agreed to make corrections to these types of investigations. Ms. Harris told me regarding this conclusion "there is insufficient rationale to make the conclusion." Additionally, the root cause was not justified in this instance.

B) Please refer to Exhibit EMM 13 for a copy of Unplanned Deviation PR, No: 88510, (opened March 2, 2011) investigating complaint 10656633 of mixed Excedrin Extra Strength caplets, Lot: 10099302 with Excedrin ES Gelcaps.

The investigation into this complaint concluded, in part, "Based on all the supporting evidence above, there is a very small to no possibility that the foreign product was introduced through Novartis procedures and practices."

The evidence in the investigation shows that the two products inside the complaint sample were packaged on the same equipment (line (b) (4)) consecutively on the same day (10/4/10). Please refer to page 4 of Exhibit EMM 13 for a line (b) (4) usage log showing how the two products in the complaint mix-up were packaged consecutively at NCH-Lincoln.

Because the firm feels there is a "very small to no possibility" for this type of mix-up to occur within their control, they did not extend the investigation to other lots. **This is a recurring problem at this firm.**

Management told me they understood my concerns and agreed to make corrections to these types of investigations. Additionally, no root cause was determined in this instance.

OBSERVATION 4

An NDA-Field Alert Report was not submitted within three working days of receipt of information concerning an incident that caused a drug product or its labeling to be mistaken for another article.

Specifically,

You have failed to file NDA Field Alerts within 3 days of a problem being identified.

You have received numerous consumer complaints which were not submitted to the FDA as required by your firm's procedures:

For example:

A) Since October of 2010 (a period in time where second person review of consumer complaints ceased at your firm), there have been 21 consumer complaints (for NDA products) that procedurally should have been reported as 3 day Field Alerts. A review of two individual Technical Complaint Investigation Reports for two of these NDA mix-up complaints (case 10642591 and case 10675854) revealed your investigation and conclusion (justification) for not submitting 3 day Field Alerts was inadequate. **Also, these two reports are indicative of a pattern of problem at your firm.**

It should be noted that this number was only verified beginning from October 2010, but is indicative of a problem for all consumer complaints received by your firm for mixed solid dosage form products on the market.

B) You have failed to file a 3 day Field Alert as required by your procedure, for complaint 10650826 regarding a mix-up of Excedrin Migraine Caplets, received on 1/26/11. The complaint sample was received by your firm on 2/14/11 and confirmed on 2/16/11. However, your initial 3 day Field Alert was not submitted until 2/22/11.

It should also be noted the conclusions drawn into the investigation of this mix-up did not appear to be supported by evidence gathered during the investigation. (See Observation 8-C)

C) You failed to file a 3 day Field Alert as required by your procedures, for complaint 10642060 regarding a mix-up of Excedrin Migraine Geltabs (lot: 10039449), received on 1/5/11. The complaint sample was received by your firm on 2/1/11 and confirmed on 2/4/11. However, your initial 3 day Field Alert was not submitted until 2/8/11.

Additionally, this complaint involves a mix-up of Excedrin Migraine Geltabs, Lot: 10096621, expires: 7/12 and Excedrin Migraine Tablets, Lot: 10039449, expires 7/10. The carton in question (Excedrin Migraine Geltabs, Lot: 10096621, expires: 7/12) was not reported as required by your 3-day Field Alert procedures (all lots potentially affected in the complaint were not addressed in the Field Alert, dated 2/8/11)

A further review of your firm's complaint file revealed Excedrin Migraine Tablets, Lot: 10039449 (same lot as above) had a second mix-up complaint on 4/2/08 that appeared to have an unsupported conclusion.

Your firm's procedure, SOP-202335, OTC NDA Field Alert Reports, dated 7/31/09, reads in part, "Reports must be submitted to district FDA offices within three (3) days of a problem being identified. The three (3) day timing starts when the firm becomes aware of a reported problem (ie. complaints or internal testing)."

Discussion with Management:
(Written by EMM)

A) Please refer to Exhibit EMM 14 for OTC NDA Field Alert Reports, SOP-202335, dated 7/31/09. Page 3 of this Exhibit reads, in part, "The three (3) day timing starts when the firm becomes aware of a reported problem (i.e. complaints or internal testing").

Exhibit EMM 23 shows a list of every complaint the firm has received for "foreign product" since January 2009. Beginning on page 31 of this Exhibit, I chose to mark pink highlights next to NDA products that have complaints that have not been fully reviewed by Quality Assurance. These are all instances, according to procedures currently in place, which should have been reported as 3-day field alerts.

Additionally, initial complaint investigations opened and closed in two instances are inadequate.

For example:

Please refer to Exhibit EMM 16 for a copy of the firm's investigation into case # 10642591. Excedrin Migraine caplets, lot 10095209, were received back to NCH-Lincoln from a complainant that also contained 2 red and white capsules. In this instance the two red and white capsules were never identified.

The investigation into what these two red and white capsules are is inadequate in that the investigation reads, in part, "Drugs.com was unable to identify this product."

I asked Ms. Harris if using "Drugs.com" as the sole source for unidentified tablet identification was written in procedures and she told me "No". I explained to her that given the number of these complaints Novartis receives (foreign tablets), they should have a procedure in place for attempting to identify unknown tablets/capsules/gelcaps, etc.

Management told me they understood my concern and promised to make corrections.

Please refer to Exhibit EMM 17 for a copy of the firm's investigation into case # 10675854. In this instance, a sample of prevacid, lot: 23822004 was returned to NCH-Lincoln from a complainant on 5/2/11. The investigation reads, in part, "small amount of unknown brown liquid substance" was inside the bottle.

The investigation, shown in Exhibit EMM 17, is deficient in that there is documentation to show the unidentified brown substance had attempted to be identified. Furthermore, there is no mention that of where this brown substance may have come from.

I told Ms. Harris, at a minimum, the brown substance should be addressed. I asked her, "Do you use brown liquid in your manufacturing process?" Additionally, there is no root cause identified for this complaint investigation.

Ms. Harris told me Novartis does not use a laboratory for analysis of unidentified substances or solid dosage forms. (There is no procedure requiring identification)

It should be noted that these two Technical Complaint Investigation reports are examples taken to show a recurring problem at this firm.

B) Please refer to Exhibit EMM 18 for a copy of the firm's Unplanned Deviation (87817), Field Alert dated 2/22/11, and Technical Complaint Investigation record for a complaint regarding foreign product found in a container of Migraine Caplets.

This complaint was received by NCH-Lincoln on 1/26/11. The complaint sample was received by NCH-Lincoln on 2/14/11, confirmed on 2/16/11, however the initial 3 day Field Alert was not submitted until 2/22/11. This is outside of the three days as required procedurally.

It should also be noted that the conclusions drawn in the investigation into this mix-up were not supported by evidence gathered during the investigation. (See Observation # 8-C)

C) Please refer to Exhibit EMM 19 for a copy of the firm's Unplanned Deviation (87756), Field Alert dated 2/8/11, and Technical Complaint Investigation record for a complaint regarding foreign product found in a container of Excedrin Migraine Geltabs.

This complaint was received by NCH-Lincoln on 1/5/11. The complaint sample was received by NCH-Lincoln on 2/1/11, confirmed on 2/4/11, however the initial 3 day field alert was not submitted until 2/8/11. This is outside of the three days as required procedurally.

In this in instance, the carton in question, Excedrin Migraine Geltabs, Lot: 10096621, expires: 7/12, was not reported at all as required by 3-day field alert procedures (all lots potentially affected in the complaint were not addressed in the field alert, dated 2/8/11)

A further review of the firm's complaint file revealed that Excedrin Migraine Tablets, Lot: 10039449 (same lot as above) had a second mix-up complaint on 4/2/08 that has an unsupported conclusion (see page 24 of Exhibit EMM 19). Specifically, the conclusion reads, in part, "it is possible that the consumer is expecting the Migraine tablets to be different in appearance since the name is not the same on the bottles." There is no documentation in the investigation that this statement was verified.

OBSERVATION 5

The batch records do not record the distinctive identification number, code, and name of equipment to identify major equipment to show the specific equipment used in the manufacture of a batch of a drug product.

Specifically,

You have failed to document the distinctive identification of the slats utilized on the (b) (4) tablet fillers during packaging operations on non-dedicated packaging Lines (b) (4) and (b) (4) (Lines (b) (4) and (b) (4) are used to package products such as Excedrin tablets, caplets, gel tablets, Bufferin, and No doz) (Line (b) (4) is used to package DEA schedule II products such as (b) (4) and (b) (4) solid

dosage forms)

This is important because the dedicated slats are utilized as supporting evidence in two of your complaint investigations. These investigations (identified as Unplanned Deviation Report 74956 and 73243) state in part:

> "...The cavities in the slats are dedicated to a specific size product dose. The cavities in the slats used for Excedrin caplets are too small to hold Excedrin tablets. If Excedrin tablets had been in with the bulk caplets, they would have remained in the hopper. The packaging equipment used does not support this complaint."

This conclusion is based on knowing which dedicated slat was used in production (there are (b) (4) different sets of dedicated slats which can be utilized in packaging Lines (b) (4). However, there was no documentation in the batch record of the dedicated slat used to package batch records 10074660 and 10066070, which are associated with Deviation Reports 74956 and 73243, respectively.

Furthermore,

From 1/1/09 to 6/26/11, there have been (b) (4) bottles packaged on Line (b) (4) (b) (4) bottles packaged on Line (b) (4) and (b) (4) bottles packaged on Line (b) (4). According to a Novartis Quality Manager, none of these bottles have documented traceability to a particular set of slats.

Discussion with Management:
(Written by JRL)

Slats, utilized in the (b) (4) fillers, are used to transfer product from the hopper to the bottle. The slats are placed and configured into (b) (4) tablet fillers depending on the solid oral dosage form and bottle quantity. The slats carry the correct count of product from the hopper to the bottles. These slats have different depths, sizes, and configurations which are unique to each solid dosage form size and shape. There are (b) (4) unique sets of slats utilized on packaging line (b) (4), (b) (4) unique sets of slats which can be utilized on packaging line (b) (4) & (b) (4), and (b) (4) set which is only utilized only on packaging line (b) (4) The slats are stored in drawers in the mezzanine area over its respective packaging line. These drawers are identified with each name of the unique slat associated with a particular solid oral dosage form (See **Exhibit JRL 9, pages 6-8**).

The firm investigated complaint 10475192 and 10506228 under unplanned deviation reports 73243 (**Exhibit JRL 12**) and 74956 (**Exhibit JRL 13**) (respective to complaint number). These two investigations used the following information to support their conclusions:

Unplanned Deviation 73243 reads in part (**Exhibit JRL 12**, page 2, 2nd paragraph from the bottom):

"***The cavities in the slats are dedicated to a specific size product dose. The cavities in the slats used for Excedrin caplets are too small to hold Excedrin tablets. If Excedrin tablets had been in with the bulk caplets, they would have remained in the hopper. The packaging equipment **used** does not support this complaint.***'

Unplanned Deviation 74956 reads in part (**Exhibit JRL 13**, page 2, 2nd paragraph from the bottom):

"***The cavities in the slats are dedicated to a specific size product dose. The cavities in the slats used for Excedrin caplets are too small to hold Excedrin tablets. If Excedrin tablets had been in with the bulk caplets, they would have remained in the hopper. The packaging equipment **used** does not support this complaint.***"

The firm does not uniquely identify the slats utilized in their packaging operations on packaging lines (b) (4) and (b) (4). None of these three packaging lines are dedicated to one product. Slats are exchanged on a (b) (4) basis depending on the bottle quantity and solid oral dosage form. Furthermore, without uniquely identifying each slat, the slats utilized during a packaging campaign cannot be identified in the batch record.

I asked Polly Harris, QA Supervisor, if the identification of slats were recorded in batch records for packaging. She informed me the identification of slats has never been documented in the batch record. It would appear to be impossible to use the slats as supporting evidence for a mix-up complaint, if the unique slat is not identified in the batch record at the time of packaging.

From 1/1/09 to 6/26/11, there have been (b) (4) bottles packaged on Line (b) (4), (b) (4) bottles packaged on Line (b) (4) and (b) (4) bottles packaged on Line (b) (4). This was evidenced by the firm on **Exhibit JRL 14**. None of these bottles can be traced to a particular packaging slat.

OBSERVATION 6

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

Specifically,

Your Quality Assurance review of critical foreign tablet complaint investigations (Technical

Complaint Investigation Reports) is not occurring in a timely manner.

A review of foreign tablet complaint investigations, received by your firm, since 1/1/2009, revealed a total of **367 of 401** critical Technical Complaint Investigation Reports, have not been second-person reviewed within (b) (4) days as required by your procedures.

There are approximately 138 reports that took over 100 days to review.

According to your procedures, closure (including QA review) of individual complaint investigations should be completed within (b)(4) days of receipt for all critical complaints (per Complaint Handling Procedure, SOP-202313).

Discussion with Management:
(Written by EMM)

Please refer to Exhibit EMM 15. These are foreign product complaints received by the firm from 2009-current (2011). To the right of the pages in the Exhibit is a column reading "Days from Created to Reviewed". I chose to highlight this area in green for ease of viewing. Any number in this column above (b)(4) days is outside of the firm's current procedure.

A review of foreign tablet complaint investigations received by the firm, revealed a total of **367 of 401** critical Technical Complaint Investigation Reports, since 1/1/2009, have not been second-person reviewed within (b) (4) days as required.

Ms. Harris told me they were unaware how far behind their Quality Unit was regarding review of complaints.

Mr. Delaney then told me Novartis is going to hire/transfer additional trained QA personnel to conduct further reviews of complaints received to this facility for all products within expiry. No specifics were discussed.

OBSERVATION 7

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

Specifically,

You have failed to identify the root cause of customer complaints for solid dosage form foreign tablets of products manufactured at your firm since at least 2009.

Since 2009, you have received approximately 57 returned customer complaint, mix-up samples containing only NCH-Lincoln produced product.

Despite the continued evidence of solid dosage form mix-ups over these years, you have not determined a root cause of tablet/capsule/geltabs mix-ups.

As an example of the above,

A) You have failed to justify the root cause for a recent mix-up complaint of Excedrin Migraine Tablets, Lot # 10087498, mixed with Excedrin Migraine caplets.

The direct cause was identified as "Occurred outside Novartis Lincoln Control", however, there is no evidence to support your root cause. **This is just one example (showing a pattern) in which the root cause of the mix-up was determined to occur outside Novartis Lincoln control without documented justification.**

Lastly,

Your conclusion reads in part, "**based on this investigation, it is not possible that the products were mixed within Novartis control."

However, a review of the investigation into this problem revealed Excedrin Migraine Caplets were packaged on the same line b(4) four orders prior to Excedrin Migraine Tablets, Lot: 10087498, and immediately after.

B) You have failed to justify the root cause determination for a recent mix-up complaint of Excedrin Migraine Gel Tabs, Lot # 10072553, mixed with Excedrin TH Express Gels.

You have concluded, "The only possible way that the Excedrin TH Express gel caplets to have ended up inside the Excedrin Migraine GelTabs was for it to happen after the customer had opened the bottle." However, there is no documented evidence to support this root cause.

THIS OBSERVATION DEMONSTRATES A PATTERN OF PROBLEMS AT YOUR FIRM.

Discussion with Management:
(Written by EMM)

Please refer to Exhibit EMM 12 for a copy of the firm's complaint investigation report, NDA Field Alert, and unplanned deviation report into a recent mix-up complaint of Excedrin Migraine Tablets, Lot # 10087498, mixed with Excedrin Migraine caplets.

The conclusion on page 8, reading in part, "This incident is believe to have occurred outside of the manufacturing, packaging and holding operations based on this investigation it is not possible that the products were mixed within Novartis control."

There is no documentation for this (or any mix-up attributed as occurring outside of Novartis control) to show this has ever been investigated. For example, complainants are not questioned as to the possibility of it happening within their control. Also, the Novartis distribution chain has never been evaluated during any investigation into this recurring problem.

I asked Ms. Harris "Has Novartis ever conducted an investigation outside of this plant. For example, have you ever questioned your distributors/warehouse personnel about this problem? (mixups)" She said "no". I told her the above is just one example where Quality Assurance concludes mix-ups occur outside of their control, yet there is no justification for this continued assumption.

Ms. Harris told me on 6/14/11, "We do not understand the large number of mix-up complaints we have. We can not reproduce this internally."

Please refer to Exhibit EMM 20 for a copy of the firm's complaint investigation report, NDA Field Alert, and unplanned deviation report into a recent mix-up complaint of Excedrin Migraine Geltabs, Lot # 10072553, mixed with Excedrin TH Express Gels.

Page 6 of this Exhibit summarizes the conclusion, reading in part, "The only possible way that the Excedrin TH Express gel caplets to have ended up inside the Excedrin Migraine GelTabs was for it to happen after the customer had opened the bottle."

In this instance, there is no justification to support this conclusion (customer and distribution chain was not investigated). Also, a review of the records shows two pieces of equipment in common between these two products, the bonner bin and packaging line.

Despite, the fact that these products are packaged on the same line and use the same bins, the firm concludes, in part, "It is not possible for the Excedrin TH Express gel caplets to have ended up inside the Excedrin Migraine GelTabs bottle at the Lincoln site."

Management told me they understood and promised to make corrections to past and future complaint investigations. Details can be seen in Exhibit EMM 5 (corrections proposed)

OBSERVATION 8

Written records of investigations into unexplained discrepancies do not always include the conclusions and follow-up.

Specifically,

Your Unplanned Deviation Reports are deficient in that conclusions drawn are not supported by the evidence in the reports.

For example,

A) The conclusion for Unplanned Deviation PR, No: 83756 (opened 10/20/10 and approved 10/22/10 for foreign tablets inside of Prevacid 24 hour packages) is not supported by evidence documented in the report.

The conclusion reads, in part, "Product pilfering is the most likely cause***Deliberate***Cause Verified". Additionally, the summary reads in part, "it appears the package was pilfered outside of Novartis' control." It also states, in part "it appears the carton was resealed/reglued and returned to the retailer for refund with Prevacid tablets being replaced with acetaminophen tablets. The suspect package was subsequently placed back on the shelf and purchased by the noted complainant."

A review of your investigation revealed there was no evidence to support the root cause (above) and conclusion that the sample was "pilfered".

B) Your conclusion for Unplanned Deviation PR, No: 88510 (opened March 2, 2011, investigates complaint 10656633 of mixed Excedrin Extra Strength caplets, Lot: 10099302 with Excedrin ES Gelcaps) is not supported by the information in the investigation.

Your conclusion reads in part "Based on all the supporting evidence above, there is a **very small to no possibility** that the foreign product was introduced through Novartis procedures and practices."

Further review of the information in the report indicated both products in the complaint (Excedrin Extra Strength Caplets and Excedrin ES Gelcaps) were packaged by NCH-Lincoln on the same

equipment (line (b) (4) in the firm) consecutively, on the same day 10/4/10. This information does not support your summary.

C) Your conclusion for Unplanned Deviation PR No: 87817 (opened 2/16/11, investigates complaint 10650826 of mixed Excedrin Migraine caplets, Lot: 10101757 with Excedrin Migraine Tablets) is not supported by the information in your investigation.

Your conclusion reads in part "This event occurred outside of Novartis control.", also "The incident is believed to have occurred outside of the manufacturing, packaging and holding operations at Novartis based on this investigation it is not possible that the products were mixed within Novartis control."

There is no documented investigational evidence to support your statement "This event occurred outside of Novartis Control". The product in the returned sample was packaged at NCH-Lincoln on line (b) (4) within 3 days of each other (11/17/10 and 11/20/10). Additionally, your investigation also revealed several areas in the process flow where the product could have come into contact (compression, film coating. Transport bins, packaging).

THE ABOVE EXAMPLES REPRESENT A PATTERN OF PROBLEM AT YOUR FIRM WHERE INVESTIGATION CONCLUSIONS ARE MADE WITHOUT JUSTIFCATION.

Discussion with Management:
(Written by EMM)

Please refer to Exhibit EMM 21. This is the firm's unplanned deviation report (83756), and Technical Complaint Investigation Report for a Prevacid complaint of foreign tablets in the bottle.

Please read page 1 and 2 of Exhibit EMM 21 for details of the complaint. The complaint sample was received by Novartis and examined on 10/20/11. The report reads, in part, "The unit carton appears to have been re-glued in a small area as it has discolored the unit carton-the end corner of the carton can be lifted and you can see where the original adhesive was present. It is possible this may be a case of pilfering."

I asked Ms. Harris what "pilfering" meant to her, and she said "stealing".

The conclusion reads "It appears the carton was resealed/reglued and returned to the retailer for refund with Prevacid tablets being replaced with acetaminophen tablets. The suspect package was subsequently placed back on the shelf and purchased by the noted complainant."

I asked Ms. Harris if they had any documented evidence to justify the above statement is correct. She said "no". I also asked her if Novartis had contacted the store (above) that "subsequently placed back on the shelf" the Prevacid bottle. She said "no".

When I questioned Ms. Harris (who signed this investigation as acceptable on 10/22/10) about this conclusion that has no documented investigation, she said "We made a speculation that we didn't have any evidence for."

I told her in this instance, NCH-Lincoln failed to follow investigation procedures.

Specifically, page 14 of Exhibit EMM 8 (SOP-202891) reads:

Write a conclusion to the deviation that includes the following:

- A clear assessment of the impact of the deviation on product or process quality.
- A product decision with clear justification for decisions and actions.
- A description of potential impact on product registrations.

In the instance of deviation 83756, the above criteria were not addressed.

B) Please refer to Exhibit EMM 13. This is the firm's unplanned deviation report (88510), and Technical Complaint Investigation Report for complaint details of mixed Excedrin Extra Strength caplets, Lot: 10099302 with Excedrin ES Gelcaps. Please read pages 1 and 2 for details of the firm's investigation.

Page 2 reads of this investigation reads, in part, "Based on all the supporting evidence above, there is a **very small to no possibility** that the foreign product was introduced through Novartis procedures and practices."

The investigation documents how the two products in the same bottle (complaint sample) were packaged on the same line consecutively (on 10/4/10). I told Ms. Harris that this information does not support "there is a very small to no possibility that the foreign product was introduced through Novartis procedures and practices."

Additionally, the conclusion reads in part, "There is no possibility to deliver an odd number of product as there are [redacted] pieces of product per slat delivered at one time." This portion of the operation is monitored by a single operator who is looking at empty slats. The statement that there is "no

possibility" can not be justified. Additionally, the firm does not identify which slats were used on packaging records. (see Observation 5 for details).

Ms. Harris told me she understood and Mr. Delaney promised they would re-review all complaints.

C) Please refer to Exhibit EMM 18 Unplanned Deviation PR No: 87817 investigating complaint 10650826 of mixed Excedrin Migraine caplets, Lot: 10101757 with Excedrin Migraine Tablets.

Page 4 of this Unplanned Deviation reads under Root Cause: "This event occurred outside of Novartis control." This root cause reads as a statement of fact that it occurred outside of their control. However, nowhere in the documentation is there investigational evidence to show this to have occurred outside their control. For example, the customer was not contacted, nor was the distribution chain ever questioned.

From my review, the product in the returned sample was packaged at NCH-Lincoln on line (b) (4) within 3 days of each other (11/17/10 and 11/20/10). Additionally, the investigation also reveals several areas in the process flow where the product could have come into contact (compression, film coating. Transport bins, packaging).

Drawing conclusions without documented evidence to support the statement is a recurring problem at this firm (regarding handling complaints of "foreign tablets").

The above examples are indicative of how this firm handles complaints of this nature.

OBSERVATION 9

Written procedures describing the handling of complaints do not include provisions for review by the quality control unit of any complaint involving the possible failure of a drug product to meet any of its specifications, a determination as to the need for an investigation of any unexplained discrepancy, and explaining the reasons for the failure of the batch or any of its components to meet specifications.

Specifically,

Your Quality Assurance Unit has consistently failed to review critical complaints for drug products manufactured and packaged at your facility.

For example,

2011:

223 critical complaints have not been properly reviewed out of 223 critical complaints received by your firm.

2010:

165 critical complaints have not been properly reviewed out of 587 critical complaints received by your firm.

Also, your Quality Assurance review of critical complaints ceased in mid-October of 2010. This deficiency was unnoticed by your Quality Unit until this FDA inspection.

Specific to Foreign Product Complaints:

Since October of 2010, a total of 88 consecutive critical complaints of foreign tablet complaints have not been adequately reviewed or investigated by your Quality Assurance Department.

In this instance, your Complaint Handling Procedure SOP-202313, and Quality Manual, Module N14.3 were not followed.

Discussion with Management:
(Written by EMM)

Please refer to Exhibit JRL 17. This is a CD containing all NCH-Lincoln product quality complaints (including critical, major and minor complaints) received for the years 2009-2011. A review of this information revealed a total of 223 critical complaints in 2011 that have not been reviewed by a second person in the Quality Assurance department. In 2010, 165 critical complaints have not been second-person reviewed.

Please refer to Exhibit EMM 22. This is the firm's complaint handling procedure, SOP-202303, dated 5/20/09. Page 10 of this Exhibit directs the firm, in part, to "Close critical complaints within (b) (4) calendar days from the date of receipt." It is important to understand that in order to close an investigation adequately, a second person Quality Assurance review is required. On over 300 compliant investigations since 2009, this has not occurred.

I asked Ms. Harris why review of critical complaints is consistently (for years) not occurring at this facility. She told me "they are behind". I understood this to mean that the Quality Assurance analysts within NCH-Lincoln are not reviewing complaints due to time constraints. Additionally,

Ms. Harris told me she was not aware of this problem until this FDA inspection.

Please refer to Exhibit EMM 23. This shows every complaint received by NCH-Lincoln for "foreign product" since 2009. The columns towards the top of this Exhibit show information about the complaint. I chose to highlight in blue columns for "Case Review Date", additionally Days from Created to Originally Closed". Beginning on page 30 of this Exhibit shows blank columns under "Case Review Date". In these instances, beginning in late September 2010, there have been no Quality Assurance Reviews of these critical complaints (see yellow highlights).

Ms. Harris told me she was unaware how far behind the Quality Unit is regarding reviewing complaints.

Mr. Delaney told me they are going to hire additional staff to assist in the corrective actions as a result of this inspection.

OBSERVATION 10

Procedures describing the handling of written and oral complaints related to drug products are not written or followed.

Specifically,

A) Your Quality Directive 2.1.01, Management Escalation Process, is routinely not followed.

For example, your site is procedurally obligated to report to Global QA "Any (critical) complaint or adverse event that may result in a potential 3 day Field Alert, BPDR, recall, correction or market withdrawal or may require non-routine regulatory reporting."

This procedure has not been followed, as Novartis corporate personnel was not aware (for a minimum of the last two years) of your critical complaints regarding complaint mix-ups until early June of 2011.

B) You have failed to send postage-paid mailing materials to customers complaining of foreign tablets (considered "critical" by your firm) as required procedurally by SOP, 203133, version 1, dated 1/22/10.

In 2011, a total of 5 instances occurred where postage-paid materials were not sent to complaining

customers when deemed necessary.

In 2010, a total of 13 instances occurred where postage-paid materials were not sent to complaining customers when deemed necessary.

This is significant, because neglecting to ship the postage-paid materials to the complainant expunges any attempt for the suspect product to be returned and properly investigated by your firm.

It is important to understand also that no person in Novartis was aware of this failure until the information was requested by the FDA on 6/16/11.

OTHER PROCEDURES CONSISTENTLY NOT FOLLOWED INCLUDE:

C) Complaint handling Procedure, SOP-202313, dated 5/09, was not followed in that critical complaints were not reviewed and investigations are not conducted as required.

D) Deviation Investigation Procedure, SOP-202891, dated 6/10, was not followed in that investigations were not always opened as required, all lots/batches of product potentially affected were not determined, conclusions were not justified and root cause was routinely not identified (regarding foreign tablet mix-ups).

E) Quality Manual for Handling of Consumer Complaints, Module N14.3, was not followed in that critical complaints were not reviewed or approved as required. Additionally, adequate corrective and preventative actions were not addressed and followed up (regarding foreign tablet complaints).

Discussion with Management:
(Written by EMM)

A) Please refer to Exhibit EMM 24. This shows the firm's Quality Directive "Management Escalation Process". Page 17 of this Exhibit shows a chart for escalating known problems to upper management in the firm. This states that "Any (critical) complaint or adverse event that may result in a potential 3d field alert, BPDR, recall, correction or market withdrawal or may require non-routine regulatory reporting."

The consumer complaints that have not been reviewed by the firm (shown in Exhibit EMM 9 and described in Observation 2 above) were not escalated to appropriate divisions within Novartis.

This is evidenced by the fact that Ms. Arencibia told Investigator Lambert and I (on 6/22/11) that corporate was not aware of the foreign tablet mix-up complaints and problems at this facility.

I asked Ms. Harris why NCH-Lincoln wasn't following their escalation process procedure and she told me there was a miscommunication. She told us not every complaint was escalated as required according to Quality Directive 2.1.01 (Exhibit EMM 24).

B) Please refer to Exhibit EMM 25 for the procedure "Guidelines for Requesting Customer Complaint Product from the Consumer", SOP-203133, dated 1/22/10. Page 3, towards the bottom, reads in part Postage-paid mailing materials are sent to the consumer for product return (for critical and major complaints).

Exhibit EMM 26 shows a summary of foreign product complaints and information about when the customer was shipped a postage-paid mailer. On 16 instances since 2009, customers complained of foreign tablets and no postage-paid mailing materials were sent.

This is important because the firm does not further investigate instances where product does not get returned. In these instances, no further investigation was conducted.

Mr. Delaney told me they didn't realize this procedure wasn't always followed. Corrections were promised, but details were not discussed.

OTHER PROCEDURES CONSISTENTLY NOT FOLLOWED INCLUDE:

C) Complaint handling Procedure, SOP-202313, dated 5/09, was not followed in that critical complaints were not reviewed and investigations are not conducted as required. Please refer to Exhibit EMM 22.

D) Deviation Investigation Procedure, SOP-202891, dated 6/10, was not followed in that investigations were not always opened as required, all lots/batches of product potentially affected were not determined, conclusions were not justified and root cause was routinely not identified (regarding foreign tablet mix-ups). Please refer to Exhibit EMM 8.

E) Quality Manual for Handling of Consumer Complaints, Module N14.3, was not followed in that critical complaints were not reviewed or approved as required. Additionally, adequate corrective and preventative actions were not addressed and followed up (regarding foreign tablet complaints). Please refer to Exhibit EMM 28.

OBSERVATION 11

The number of qualified personnel is inadequate to perform and supervise the manufacture, processing, packing, and holding of each drug product.

Specifically,

There are an inadequate number of personnel conducting and reviewing (at a minimum) complaint investigations occurring at your firm.

This was evidenced in your firm's lack of review of critical complaints as required procedurally.

This was also evidenced by the fact that once the deficiencies were discovered (during this FDA inspection), you brought outside assistance to conduct the reviews which should have originally been done by your Quality Assurance staff at NCH-Lincoln.

Also, you have one person (or designee in absence) conducting and closing initial complaint Technical Complaint Investigation Reports. This is inadequate as evidenced by failing to open b(4) investigations when needed, developing conclusions not supported by evidence, and consistently failing to follow up complainants when necessary.

Discussion with Management:
(Written by EMM)

This inspection revealed the firm currently has one person in the quality unit who is assigned to review and conduct initial complaint investigations (in the (b) (4) system). This was shown in the above Observations to be insufficient as evidenced by the above deficiencies.

I spoke with Ms. Harris about this problem, and she told me she agreed they had deficiencies and were going to work on them.

I then asked her "Do you feel you have the time, resources (personnel) and training to execute your procedures effectively?" She said, for the short term, they were going to rearrange personnel and roles, but for the long term "No".

She told me on 6/17/11 that NCH-Lincoln was going to bring in additional resources and hire more

Quality personnel in order to complete the commitments shown in Exhibit EMM 5.

OBSERVATION 12

GMP training is not conducted with sufficient frequency to assure that employees remain familiar with CGMP requirements applicable to them.

Specifically,

Training is inadequate in the Quality Unit at your firm.

This is evidenced by the problems documented: failure to open (b) (4) investigations when needed, investigational conclusions not supported with evidence, failures to satisfy 3-day Field Alert requirements, failure to escalate critical complaints to corporate personnel, failure to notify top management when Quality procedures are not being followed due to time constraints, and consistent failures to follow up with complainants when necessary.

Most importantly, a lack of training is evidenced by the fact that no person at NCH-Lincoln recognized the failures in the Quality Unit's Oversight (see Observations above) prior to this inspection.

Discussion with Management:
(Written by EMM)

The training provided by this facility is inadequate as evidenced by the Quality Unit's consistent failure to follow procedures. Specifically, regarding failures to open investigations when needed, conclusions not supported with justification, failure to file 3-day Field Alerts as required, etc. (see Observations above for further details)

Additionally, no person at NCH-Lincoln recognized the failures in the Quality Unit's oversight prior to this inspection.

Ms. Harris told me she agreed with this observation and would work to make corrections. Specifics can be seen in Exhibit EMM 5.

OBSERVATION 13

Written records of major equipment cleaning, maintenance, and use are not included in individual equipment logs.

Specifically,

Your Use Sequence Log, used to document packaging activity on non-dedicated equipment (line (b) (4)), is not always completed by your operators assigned to verify packaging line clearance.

There is no operator signature in the Use Sequence Log for "Dates of Major (wet) clean only" indicating major cleans are conducted as required after a particular packaging run. Major cleans should have been documented on the forms after: Excedrin ES Tablets (6/10/09), Excedrin AFTH (6/11/09), Excedrin PM Capsules (6/18/09) however, this was not completed.

The example above is indicative of how your firm currently operates with regard to filing out line usage logs for all packaging lines.

Discussion with Management:
(Written by EMM)

Please refer to Exhibit EMM 27. This is four pages of the firm's usage sequence log for line (b) (4), which is a non-dedicated packaging line. On the left of the pages in the Exhibit are the products packaged on the line. To the right are the dates of the major cleans supposed to be verified and signed off on the usage log.

I chose to highlight on the pages where products were packaged and the cleaning of the equipment should've been verified and documented on the form, but was not.

It should be noted that the above (line (b) (4) usage log) is indicative of a problem for all packaging lines at this facility. It should also be noted that the timeframe I chose (in Exhibit EMM 27) was chosen just as an example of how the firm routinely fills out packaging equipment usage logs.

Ms. Harris told me she understood the forms were not filled out correctly by operators at NCH-Lincoln. She told me she could confirm cleaning was actually done by pulling the batch records of the lots in question. I told her in my opinion, this form should be filled out correctly by the operator who is supposed to verify the cleaning of the equipment was complete at the time it was done.

Ms. Harris told me she understood and would make corrections in the future. No specifics were discussed.

REFUSALS
(Written by EMM)

Ms. Harris declined to read or sign the affidavits presented to her by Investigator Lambert on 7/8/11.

GENERAL DISCUSSION WITH MANAGEMENT
(Written by EMM)

Throughout the course of the inspection, I updated Mr. Delaney and Mr. Walsh with the deficiencies identified. Each time, they told me the understood the problems (above) and promised to make corrections as soon as possible.

Ms. Harris told me outside consultants were hired and I was given a business card for (b) (4) (b) (4) located in (b) (4)

During the closeout meeting on 7/8/11, management told us they understood the deviations and promised a written response to the district within 15 days. The following employees were present at the closeout meeting:

Polly A. Harris, Director QA and Compliance
Joseph T. Delaney, QA Head, American Region
Terry L. Maynard, Business Development Leader
David W. Lueckenhoff, Operations Leader
Joel (MIUNK) Padin, Human Resource Leader
Terence J. Walsh, Site Leader
Carl (MIUNK) Counts, Executive Director Global QA
Vivianne (MIUNK) Arencibia, VP and Global Head, Group Compliance and Audit (via telephone)

I warned Mr. Walsh of his responsibilities to comply with the FD&C Act as failure to do so may result in FDA enforcement actions, such as: Warning Letter, Seizure, Injunction and criminal penalties.

SAMPLES COLLECTED

Sample DOC 651311 This documentary sample was collected to document the interstate movement of active pharmaceutical ingredient Acetaminophen, USP, on 9/18/09. It was then manufactured into finished product (Excedrin Tension Headache Express Gels) on or about 11/3/09, and distributed into interstate delivery on 11/16/09. This lot of product received a complaint for "foreign product" found in container, which was thought to be Excedrin Tension Headache Caplets (See Exhibit **JRL 9, page 12** for photo of two products). The complainant's bottle was never returned, because it was never requested from the complainant. Investigation 92546 (**Exhibit JRL 15**) indicated Excedrin Tension Headache Caplet 50 count bottles were packaged on the same packaging line on 11/12/09 (1 day prior to the packaging of Excedrin Tension Headache Gelcaps, lot 10078599). The root cause or conclusion for this investigation had not been established.

Sample DOC 651310 This documentary sample was collected to document the interstate movement of raw ingredient, on 8/6/10. It was then manufactured into finished product (Excedrin Extra Strength Caplets) on 9/30/10, packaged on 10/4/10, and distributed into interstate delivery on 10/5/10. This lot of product received a complaint for "foreign product" found in container, which was confirmed to be Excedrin ES Gelcaps. Investigation 88510 (**Exhibit EMM-13**) indicated Excedrin ES Gelcaps were packaged immediately prior to the affected lot. The conclusion indicated there is a very small to no possibility that the foreign product was introduced through Novartis procedure and practices. The root cause of the mix-up was not determined.

VOLUNTARY CORRECTIONS

Please refer to Exhibit EMM 5 for a description of corrective actions proposed by the firm.

EXHIBITS COLLECTED

EMM 1) (b) (4) press release for voluntary recall, dated (b) (4)
EMM 2) NDA Field Alert Report for Excedrin Migraine, lot: 10066568, dated 6/29/11
EMM 3) NDA Field Alert Report for Excedrin Migraine Caplets, lots: 10080539 and 10065734
EMM4) NDA Field Alert Report for (b) (4) lot: (b) (4)
EMM5) Novartis corrective actions proposal, dated 6/21/11
EMM6) 2010 returned samples of foreign tablets
EMM 7) 2009 returned samples of foreign tablets
EMM8) Conducting Deviation Investigations, SOP-202891
EMM9)2009-2011 unreturned Foreign Product Complaints
EMM10) List of all products packaged on lines (b) (4) & (b) (4)

EMM 11) List of all products packaged on line (b) (4)
EMM 12) Investigation information for Excedrin Migraine Tablets, lot: 10087498
EMM 13)Unplanned Deviation Report 88510 for Excedrin, lot: 10097648
EMM 14) OTC NDA Field Alert Reports Procedure 202335
EMM 15) 2009-2011 Foreign Product Complaints
EMM 16) Technical Investigation Report for Excedrin, lot: (b) (4)
EMM 17) Technical Investigation Report for Prevacid, lot: 23822004
EMM 18) Investigation information for Deviation PR 87817
EMM 19) Investigation for Excedrin Migraine, lot: 10039449
EMM 20) Investigation information for Excedrin Migraine Gel Tab, lot: 10072553
EMM 21) Investigation information for Prevacid, lot: 10076322
EMM 22) Complaint Handling Procedure, SOP-202313
EMM 23) 2009-2011 Foreign Product Complaints with case reviewed dates
EMM 24) Management Escalation Process, Quality Directive 2.1.01
EMM 25) Guidelines for Requesting Customer Complaint Product from the Consumer, SOP-203133
EMM 26) Foreign product complaint packages not sent information
EMM 27) Line (b) (4) use sequence log
EMM 28) Handling of Customer Complaints, Module N14.3

JRL 1) Organizational Chart of Novartis
JRL 2) FDA 483 response letter dated 4/23/10
JRL 3) List of (b) (4) and Animal Health Products at Novartis-Lincoln
JRL 4) List of Solid Products manufactured at Novartis-Lincoln
JRL 5) List of Liquid and Cream Products manufactured at Novartis-Lincoln
JRL 6) List of customers Novartis-Lincoln contract manufactures product
JRL 7) Overhead diagram of packaging work center (b) (4)
JRL 8) Equipment list for work centers (b) (4) and (b) (4)
JRL 9) Photos of packaging work centers and product mix ups (photos were taken by the firm)
JRL10) Complaint Handling flow chart
JRL 11) SOP 202405, "Product Recall Assessment for NCH OTC", version 3.0
JRL 12) Unplanned Deviation Report 73243
JRL 13) Unplanned Deviation Report 74956
JRL 14) Email detailing the number of products packaged on each line from 1/1/09 to 6/26/11
JRL 15) Unplanned Deviation Report 92546
JRL 16) Unplanned Deviation Report 92712

JRL 17) Hardcopy CD of 2009, 2010, 2011 complaint data in Excel format

ATTACHMENTS

1) FDA 482, Notice of Inspection, issued on 6/13/11
2) FDA 482, Notice of Inspection, issued on 6/20/11 adding investigator Lambert
3) FDA 483, Inspectional Observations, issued 7/8/11
4) Copy of C/R 651310
5) Copy of C/R 651311

Eric M. Mueller, Investigator

Joseph R. Lambert, Investigator