SUMMARY

This is a comprehensive report of a limited inspection of a drug and specialty pharmaceuticals manufacturer. This directed inspection was conducted according to Program Assignment Code 56R800. The Philadelphia District Office assignment was to investigate the mislabeling on packages of some lots of grape and fruit flavored Children's Tylenol Soft-Chew acetaminophen chewable products with phenylalanine. The packages (cartons) list the incorrect amount of phenylalanine per tablet as 3 mg per 80 mg tablet. The actual amount of phenylalanine in the grape flavor is 5 mg per tablet. The fruit burst flavor's actual amount is 6 mg per tablet.

The firm has not recalled the lots affected and distributed. The firm destroyed or correctly relabeled non-distributed products. The firm also posted information of the mislabeling on its website, www.Tylenol.com. New labels, as of December 2003, contain the correct information.

By 1/12/04, the firm also plans to add a "pop-up" to major phenylketonuria (PKU) websites. If the pop-up is clicked, it will take people to the standard statement on the Tylenol.com website. Also the firm plans to post on major search engines. When people search on terms similar to PKU, the same pop-up will appear that will take them to the standard statement on the Tylenol.com website.

The previous inspection ended 7/22/03, was classified as No Action Indicated (b)(2) The current inspection ended without an FDA-483, Inspectional Observations form. There were discussions with management regarding packaging approval and labeling procedures. The firm has revised their written packaging approval (labeling) procedures in their attempts to prevent future labeling errors.

ADMINISTRATIVE DATA

Inspected firm:	McNeil Consumer & Specialty Pharmaceuticals...Inc.
Location:	7050 Camp Hill Rd Fort Washington, PA 19034-2299
Phone:	215-273-7878
FAX:	215-273-4136
Mailing address:	7050 Camp Hill Rd Fort Washington, PA 19034-2299
Dates of inspection:	12/18/2003, 12/19/2003
Days in the facility:	2
Participants:	James P. McEvoy, Investigator

My credentials were shown to and an FDA-482, Notice of Inspection, was issued to Paula J. Oliver, Senior Director, Medical and Regulatory Science. Ms. Oliver said that the most responsible person of the firm, William McComb, President, was present, but Ms. Oliver said she was designated by

Mr. McComb to accept the FDA-482. All FDA correspondence should be addressed to Mr. McComb at the address in this report's header.

RESPONSIBILITY

The incorrect labeling occurred at this site, which is responsible for approving all McNeil labeling, according to Paula Oliver. Thomas J. Markley, Senior Director Support to Marketed Products, explained what caused the mislabeling. Elizabeth Selsley, now a Senior Research Associate, pulled an incorrect, no longer used, master formula record. She used its information to prepare the Research and Development Data Sheet (Exh. 1), that she signed on 7/25/01. The incorrect information she wrote on the data sheet was "...Contains 3 mg phenylalanine per tablet..." Ms. Selsley should have used the correct current master formula record, which included the correct information of 5 mg of phenylalanine. Thomas Markley said that he did not see this error and he signed the data sheet on 7/26/01 as the R&D Manager Approver. The data sheet was also signed and approved by Janet A. Uetz on 7/27/01 who was at the time McNeil Associate Regulatory Affairs Director. The error resulted in incorrect labels being printed. The labels were used on distributed product. See **COMPLAINTS** section for the firm's investigation of the complaint.

COMPLAINTS

The firm wrote a detailed report (Exh. 2) about the incorrect labeling. The report, titled **"REQUESTED INTERIM SUMMARY REPORT FOR FDA. 12/04/03,"** summarizes the events from the receipt of the complaint to the actions taken by the firm to prevent a reoccurrence. The following information are my observations of the firm's records and verbally reported to me by various individuals of the firm.

On October 20, 2003, the firm at this site received a complaint and gave it number (b) (4) Exh. 7). The complainant reported inconsistent labeling on Children's Tylenol, Soft Chew Grape Tablets, 30 count, (b) (4) The complainant reported that the bottle label declared 5 mg of phenylalanine, but the carton declared 3 mg phenylalanine. The complainant originally reported having two units with the same discrepancy. The complainant eventually found a total of 20 cartons with the same problem. The complainant worked as a nurse for a school district. The complainant returned the affected products to McNeil.

The firm's investigation (Exh. 7) found that this lot was manufactured and **originally** packaged in Las Piedras, Puerto Rico in 2001. The firm's record review found no packaging problems with this lot. The amount of phenylalanine (5 mg) was correct on the label and matched the current formula. The firm's complaint history review of this lot revealed one other unrelated complaint. They also found no complaints of other lots of the same product for the same reason. The firm reported that the correct labeling was used to package (b) (4) **originally**.

However, in March 2002, (b) (4) was relabeled by (b) (4) (b) (4) is an approved (b) (4)

This sale was cancelled and never left (b) (4) location. The lot remained at (b) (4) So in May, 2002, this same lot was re-cartoned by (b) (4) for domestic sales. (b) (4) of the same product were also re-cartoned at the same time. There were no problems found with (b) (4) relabeling procedures. However, (b) (4) used incorrectly labeled cartons from McNeil to use in this re-cartoning operation. The cartons were actually received from (b) (4) an approved supplier for McNeil.

The firm determined that the error occurred when the Drug Facts master labels for the grape and fruit burst 80 mg and 160 mg Soft Chews were revised in late 2001. The Research and Development staff referenced outdated formulas. The incorrect amount of phenylalanine (3 mg) per tablet was entered on the Data Sheets, which were created to start the process of new labeling. The mistake went unnoticed. New bottle and carton labels were printed and sent to (b) (4) for the re-cartoning operation. Incorrect new labels were also sent to the Las Piedras and Ft. Washington, PA sites for use. The mistake was not known by the firm until its investigation of the complaint. (b) (4) sent the relabeled product to the (b) (4) sites before it was distributed to the market.

Additionally, the Las Piedras and Ft. Washington sites packaged additional lots of the two products with a different problem. The bottle and carton labels matched with respect to the declaration of phenylalanine. But those amounts differed from the product formula. The single active ingredient of acetaminophen was correct in all of the mislabeling events, according to Paula Oliver. The firm's investigation found that no other McNeil products containing (b) (4) of which phenylalanine is a component) were affected.

On November 17, 2003, all 80 mg and 160 mg lots of Children's Tylenol Soft Chews, Fruit Burst, and Grape Flavors Tablets within the control of McNeil and at the Distribution Centers were quarantined. The firm reported that they stopped distribution of the products within their control.

Paula Oliver explained that for this product, (b) (4) (Exh. 3 for address of locations) receives manufactured product from Las Piedras. (b) (4) is located in three locations, (b) (4) (b) (4) From (b) (4) the product is distributed in generally small quantities (for example, 2-10 cases per shipment) to customers. Some of the major customers are (b) (4) distribution centers, according to Gary D. Benedict, National Sales Director. This product is only shipped to customer distribution centers, not directly to retail stores. The major customers then supply their chain of stores as needed. Paula Oliver explained that this product is made according to market demand. So frequent, smaller shipments from (b) (4) are routinely made to major customers. Gary D. Benedict said that for example, (b) (4) turns over their Children's Tylenol approximately every six weeks. (b) (4) maintains a low inventory in their distribution centers, approximately two to three weeks of inventory. So (b) (4) only sends smaller shipments to retail store distribution centers on demand. Other customers usually have this product in inventory for a longer time than does (b) (4)

The incorrect labeling was also quarantined. Orders for labeling of affected products were also blocked. Chewable manufacturing was halted until the problem was fixed. Processing restarted with correct, approved labeling. The McNeil Research and Development department in Ft. Washington reviewed the (b) (4) McNeil's change control process was modified by adding a check step that will verify label changes against the current formula.

The firm's medical assessment (Exh. 4) of this issue concluded that there is no medical risk to users of the products affected by the incorrect labeling.

GENERAL DISCUSSION WITH MANAGEMENT

I requested distribution records for all lots involved in the incorrect labeling issue. Paula Oliver responded that the firm will comply with my request but this tremendous volume of records could not be obtained for at least a few days. After a discussion with the firm's management, I narrowed the focus of my request to specific lots. I requested lot numbers (b) (4) (b) (4) lots were not scheduled for destruction or relabeling. These lots expire in (b) (4)

An estimate (Exh. 5) of incorrectly labeled product remaining on the market was created by Gary Benedict. He also included an estimate of how long before each specific product will remain on the market.

Exh. 8 is a collection of the firm's records of quarantined product, as of 12/16/03, in the three distribution centers. All of these products were to be destroyed or relabeled with the correct label and distributed. The key to the three distribution centers is: (b) (4) (b) (4)

According to Paula Oliver, (b) (4) packages of affected products were produced (b) (4) Approximately (b) (4) packages were put on hold when the initial complaint sample's discrepancy was verified on (b) (4) All lots within the control of McNeil at the three distribution centers were placed in quarantine (b) (4) Distribution was stopped. Of this total, approximately (b) (4) packages were chewables in blister packages. These blister packages will be re-cartoned with corrected labeling. The remaining packages, approximately (b) (4) (chewables in bottles) were to be destroyed. Incorrect labeling inventory was placed in quarantine and will be destroyed.

I observed that the firm followed its written procedure (Exh. 10) for generating new labeling. However, the procedure allowed for an incorrect master formula record to be used. The layers of review were documented but did not prevent the error. None of the reviewers in the process prevented an inaccurate declaration of phenylalanine from finding its way on to the labeling of marketed product.

I asked Ms. Oliver if there are any quality control checks of the accuracy of the labeling beyond the Research and Development level. She said no, it is the Research and Development's responsibility. She said that once the approval order is given to the graphics department, it is too late to make a change before the labeling is printed, packaged and distributed. Andrew Falkowski, Ph.D., Director of Quality Technical Services, said that this error had never previously occurred. He said that his firm makes many label changes.

VOLUNTARY CORRECTIONS

Exh. 6 is the new corrected form for Research and Development Data Sheet for New Package Approval. Part (b) (4) (b) (4) is the corrected section.

The newly revised written procedure (Exh. 11) for new package (labeling) removed specific steps (page 3) from the "...3.3...Procedure for R&D to prepare R&D Data Sheets..." The new procedure is designed to prevent an incorrect master formula record from being used by Research and Development. Ms. Oliver said that more levels of management with high levels of technical and medical backgrounds have been added to the approval process.

Exh. 9 is representative of the corrected labeling now being used for this product line.

SAMPLES COLLECTED

Documentary sample number 221956 was collected to document the interstate distribution of the complaint lot (b) (4)

EXHIBITS

1. incorrectly prepared data sheet
2. firm's 12/4/03 report of events surrounding incorrectly labeled product
3. (b) (4)
4. McNeil's health hazard evaluations
5. estimated trade inventory
6. corrected data sheet
7. (b) (4) firm investigation
8. product remaining at dist. centers
9. labeling- corrected
10. old written procedure for approval of packaging/labeling
11. revised written procedure for approval of packaging/labeling

ATTACHMENTS
FDA-482

James P. McEvoy

James P. McEvoy, Investigator