McNeil Consumer & Specialty
Pharmaceuticals, Div. of McNeil-PPC Inc.
7050 Camp Hill Road
Fort Washington, PA 19034
3/20-22, 25-28/02, VM, YCW, JM

GEN. SPEC.
RELEASE
F# _____ DATE 5-11-10
Reviewed by: Kiyan S Bonner

SUMMARY OF FINDINGS

This Pre-approval and GMP inspection of a drug manufacturer was conducted in response to FACTS assignment ID # 1114753, Operation ID # 927410 in accordance with CP 7346.843 and 7656.002. (b) (4) (b) (4) was covered as part of the Pre-approval inspection. The firm's role in the NDA is to perform stability testing on the clinical batches of (b) (4)

The previous GMP and Pre-approval inspection was conducted from 2/9 to 3/9/00 and was classified (b) (2) The following observations were placed on a Form FDA-483, Inspectional Observations, during the previous inspection: Motrin IB Gelcap manufacturing process deviated from ANDA 73-019; inconsistencies in the batch reconciliation records; no QA failure/deviation investigations for validation batches; no hold time specifications established for Bulk Imodium AD Liquid and oral solid dosage form cores before coating; incomplete Sugar Charging System qualifications; inconsistent calibration of the load cells; no justification to support annual cleaning of (b) (4) and (b) (4) Charging System; SOP 20-MF-CB-71 was not followed; no audit trail for electronic maintenance record system; qualification protocol for the compression machine was missing; melting point apparatus was inadequate; no wavelength calibration was performed for the HPLC's in the R&D laboratory; and calibration of the IR Spectrophotometer was not adequate. Corrections instituted by the firm in response to these observations were covered during the current inspection. No deviations were observed.

No Form FDA-483, Inspectional Observations, was issued during the current inspection. The Quality and Laboratory Control Systems were covered during this inspection. All of the firm's profile classes were reviewed. Approval was recommended for the firm's role in (b) (4)

There were no samples collected during this inspection.

This report was written by Vlada Matusovsky except where noted.

HISTORY OF BUSINESS

McNeil was founded in the late 1800's as a family owned and operated retail pharmacy. In 1959 McNeil Laboratories, Inc. was acquired by Johnson & Johnson Corp. The McNeil facility in Fort Washington, PA was constructed in 1960. At the time the firm manufactured mainly prescription drug products. The firm was incorporated in the state of New Jersey in 8/27/1970.

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Manufacturing operations currently occupy approximately 375,000-sq. ft. at the Fort Washington facility. Total number of employees is (b) (4) The firm's business hours are 8:00 AM to 5:00 PM Monday through Friday. Production is conducted on 2/12 hours or 3/8 hours shift bases from 5 to 7 days a week depending on the operation.

Exhibit 1 is the firm's product list. Most of the products manufactured at the Fort Washington facility are OTC analgesics and pharmaceuticals intended for treatment of upper respiratory and gastrointestinal conditions. Motrin Suspension 100 mg/5 ml is the only prescription drug product manufactured by the firm.

According to Paula J. Oliver, Senior Director Medical and Regulatory Science, the following changes in the firm's management and/or operations have taken place since the last inspection:

- The name of the firm has changed from McNeil Consumer Healthcare to McNeil Consumer & Specialty Pharmaceuticals Division of McMeil-PPC, Inc.
- In March of 2001 William L. McComb became a President of McNeil, Fort Washington facility replacing W. Anthony Vernon.
- In December of 2000 as a result of restructuring, the Regulatory Affairs department became a part of the Research and Development department headed by Debra L. Bowen/VP of Research and Development, MD.

McNeil Consumer & Specialty Pharmaceuticals Division of McMeil-PPC, Inc. consists of two additional manufacturing sites located in Las Piedras, Puerto Rico and Round Rock, TX. In addition, there is a joint venture Johnson & Johnson/Merck site located in Lancaster, PA where McNeil is responsible for all of the manufacturing operations. Fort Washington site serves as headquarters for McNeil Consumer & Specialty Pharmaceuticals Division of McMeil-PPC, Inc.

ADMINISTRATIVE PROCEDURES/INDIVIDUAL RESPONSIBILITIES/ PERSONS INTERVIEWED

On 3/20/02 credentials were presented and Forms FDA-482, Notice of Inspection (with attachment), were issued to William L. McComb, President, who identified himself as the most responsible individual on site. Also accompanying me on this inspection were Jeen Min, FDA Chemistry Project Manager, and Yvonne C. Wood, FDA Pharmaceutical Chemist. Jeen Min was present from 3/20/02 to 3/22/02. Yvonne Wood and I were present for the length of the inspection.

According to Ms. Oliver, William L. McComb, President, is the most responsible official on site and all FDA correspondence should be addressed to him at the

Fort Washington location. Ms. Oliver indicated that Mr. McComb has the ultimate knowledge, duty and power to prevent and correct objectionable conditions. Ms. Oliver also stated that Johnson & Johnson officials are not involved in the day-to-day operations of the firm. However, their participation is warranted in matters such as major financial expenditures, plant closures, acquisition of new products, etc. Ms. Oliver identified Ralph S. Larsen, Chairman, Board of Directors, Chief Executive Officer, Chairman of Executive Committee, as the most responsible official at Johnson & Johnson Corp.

Exhibit 2 represents Organizational Charts for Johnson & Johnson Corp. and McNeil, Fort Washington facility. According to this Exhibit Mr. McComb (page 4) reports to Brian D. Perkins, J & J WW Chairman Consumer Pharm. and Nutritionals Group (page 3), who in turn reports to William C. Weldon, J & J Vice Chairman Board of Directors (page 2), who ultimately reports to Mr. Larsen. According to Ms. Oliver, all of the firm's key officials are listed on page 4 of Exhibit 2.

QA/QC department is headed by Ann C. Rademacher, Fort Washington QC/QA Plant Manager who reports to Pedro N. Juri, VP Quality Sciences and Compliance (Exhibit 2, pages 4, 5, & 6-9). David R. Bonilla, Microbiology Manager, Richard A. Fontana, Analytical QC Lab Manager, Mark Schultz, QA Tech Services Manager, and QA Manager (currently open) report to Ms. Rademacher.

According to SOP entitled "Global Pharmaceutical Quality Policies", dated 11/29/00, responsibilities of QA unit include: ensuring compliance to standards; dispositioning all finished products; establishing a system to approve or reject raw materials, intermediates, packaging and labeling; reviewing completed manufacturing records; making sure that non-conformances/deviations are investigated; approving all specifications, approving all procedures potentially impacting the quality of finished products; making sure that internal audits are performed; managing supplier audits; making sure that periodic product reviews are carried out; approving changes that potentially impact product quality; reviewing and approving all validation protocols and reports; managing complaint handling system; administering product recall/withdrawals; approving master manufacturing records; ensuring all personnel are adequately trained and training documented, etc. Responsibility of QC unit include: conducting physical, chemical, and microbiological testing for raw materials/intermediates/in-process/finished products and environmental monitoring and keeping records; ensuring all personnel are adequately trained; making sure that the necessary calibrations are carried out and records kept; making sure that the premises and equipment are maintained and records kept; making sure that method validation plans, protocols and reports are reviewed and approved; etc.

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Ms. Oliver, Ms. Rademacher, Linda S. Labinsky, Associate Director, Regulatory Compliance, William K. Witta, QA Plant Compliance Specialist, and Mr. Fontana escorted me during this inspection and referred me to the following individuals for relevant information in their respective area of expertise:

- David R. Bonilla, Microbiology Manager;
- Paul D. Bisio, Manager Contract R&D;
- Manoj N. Shah, Ph.D., Director, New Product Development;
- Lawrence R. Constable, Plant Manager;
- David H. Rogers, Principal Scientist;
- Robert D. McDermott, Information Specialist;
- Kevin A. Rausa, Manager Manufacturing Execution Systems;
- Sharon A. Strause, Information Management;
- Michael A. Vlasic, Plant Engineering Manager;
- Rose Mary A. Dollard, Project Manager;
- James S. Beahm, Sr. Research Scientist R&D;
- Anthony S. Bean, Senior Research Associate;
- Christine Wysocki, Product Complaint Specialist;
- Thomas J. Markley, Director, Support to Marketed Products;
- David P. Chevoor, Manager Solid Dose Packaging;
- Laurence A. Luberecki, Project Manager Compliance;
- Shannon Blackburn, National Buyer;
- Kitty Frenia, Liquids Processing Manager;
- A. Hakan Erdemir, Manager Project Management;
- Elizabeth Boyles, Solid Dose Processing Manager;
- Catherine M. Devine, Manager Liquids Manufacturing;
- Melissa G. Renninger, Operations Associate;
- Carla Reyes, Manufacturing Control Inspector;
- Paul Blacken, Material Services Specialist Shipping/Receiving/Warehouse Allocations;
- Taira Dugue, Chem. Weight Team Leader;
- Helene White, Chem. Weight Operator;
- Holly Bolan, Granulation Team Leader;
- Lawrence Talley, Granulation Specialist;
- Larry Graham, Production Operator;
- Reuben Bell, Liquids Packaging Team Leader;
- Brian Hill, Stability Manager;
- Sean Park, Senior Validation Engineer;
- John Walton, Jr., Electronic Batch Record Technical Facilitator.

MANUFACTURING CODES

According to SOP 20-QA-QA-007, entitled "Change Control, Issuance and Maintenance of Master Manufacturing Requisitions and Batch Records at Fort Washington", effective date 8/18/00 (Exhibit 3), the Record Review and Control (RRC) batch record clerk assigns a unique batch number to each Manufacturing Requisition (MR) issued. Batch numbers for semi-finished goods (in process material) are automatically created within the controlling system and manually assigned to the process order. The batch number for in-process material consists (b) (4) The (b) (4) represents the (b) (4) of manufacture. The (b) (4) represents the (b) (4) of manufacture. The (b) (4) character represents the (b) (4) Last (b) (4) represent the (b) (4) (b) (4) that is assigned to the semi-finished good.

According to Ms. Rademacher, batch number for finished packaging lot consists (b) (4) The (b) (4) represents the (b) (4) of manufacture. The (b) (4) represents the (b) (4) . The (b) (4) represents the (b) (4) (b) (4) (b) (4) represent the (b) (4) (b) (4) that is assigned to the (b) (4)

(b) (4) designating the (b) (4) are defined in section 5.7 of SOP 20-QA-QA-007 (Exhibit 3, page 2).

For example, granulation batch # (b) (4) means that this (b) (4) was (b) (4) (b) (4) (b) (4) (b) (4) manufactured during the (b) (4) Batch # (b) (4) means that this (b) (4) was produced in (b) (4) at (b) (4) and it was the (b) (4) (b) (4) packaged during the (b) (4)

OPERATIONS AND EQUIPMENT

According to Ms. Rademacher, the firm manufactures and packages solid and liquid oral dosage forms.

Exhibits 4, 5, and 6 represent 1st, 2nd and 3rd floor plan diagrams, respectively, of the McNeil Fort Washington facility.

Ms. Rademacher explained that the firm has undergone a series of facilities upgrades starting from 1999. Exhibit 7 lists these upgrades and their completion status. Ms. Rademacher indicated that the only outstanding physical upgrade is construction of packaging line partitions to ensure their physical separation. This project is scheduled to be completed during the 2nd quarter of 2003.

Ms. Frenia presented me with the Project Timeline for Liquids Manufacturing Facility Area # 1 (Exhibit 8). She explained that construction of the new Liquids Manufacturing area was completed in August of 2000. Ms. Frenia indicated that the qualification of production equipment and the validation of computer system that is designed to monitor and control liquids manufacturing process have been completed. Currently the firm is working on process development for Motrin and Tylenol suspensions. NDA submission for Motrin suspension production in this new area is scheduled for the 4th quarter of 2002. Validation of Motrin and Tylenol suspension processes is anticipated to commence in the beginning of 2003. Exhibit 9 represents a process flow diagram for the new liquids production area.

(b) (4)

The firm's role in (b) (4) was covered during this inspection.

According to Ms. Oliver, the firm is responsible for conducting the stability studies on (b) (4) clinical batches. Stability on the marketed product batches will be performed at J&J/Merck Lancaster, PA facility.

St. Joseph Aspirin Chewable Tablet, 81 mg

Exhibit 10 represents a process flow diagram for St. Joseph Aspirin Chewable Tablet. Exhibit 11 represents a list of processing equipment used in manufacturing and packaging of the product.

According to Ms. Boyles, St. Joseph Aspirin Chewable tablets are manufactured using a (b) (4) process. (b) (4) are (b) (4) Blender, and passed through a (b) (4) Comminutor, to make the (b) (4) blend. The lubricant system, (b) (4) are (b) (4) with (b) (4) then passed through a (b) (4) This is the (b) (4) Finally, the separate (b) (4) blends are added to a Tote bin, along with (b) (4) and blended (b) (4) The batch is then compressed on a (b) (4) tablet press using (b) (4)

Children's Tylenol Cherry Suspension

Exhibit 12 represents a process flow diagram for Children's Tylenol Cherry Suspension. Exhibit 13 represents a list of processing equipment used in manufacturing and packaging of the product.

According to Ms. Devine, the suspension in manufactured in a (b) (4) (b) (4) mix tank equipped with (b) (4) The ingredients are added to the mix tank in a defined order. Some ingredients are first incorporated into pre-mixes. These pre-mixes are used to ensure complete dissolution of ingredients such a (b) (4) and to allow for proper (b) (4) of the (b) (4) From the mix tank the suspension is transferred through the (b) (4) into a hold tank where it's intermittently mixed to maintain uniformity of the batch.

I reviewed the following documents/records during this inspection:

- Validation Protocol for (b) (4) Process # 20-VAL-PRO-C-163-7, (b) (4) Ibuprofen Suspension Packaged in 1 oz Bottles (Manufactured using (b) (4) approval date 7/7/95.
- Ibuprofen Suspension (b) (4) Process 1 oz Package Size Process Validation Report # 20-VAL-PRO-C-163-7, approval date 8/4/95.
- Non-conformance report #'s (b) (4) (b) (4)
- Consumer Complaint #'s (b) (4) (b) (4)
- Annual Product Review for St. Joseph Chewable Tablet, Orange Flavor for period starting 2/1/01 and ending 1/31/02, approval date 3/22/02.
- Annual Product Review for Children's Tylenol Suspension Cherry Flavor, for period starting 1/1/00 and ending 12/31/00, approval date 5/14/01.
- Annual Product Review for Children's Tylenol Suspension Cherry Flavor, for period starting 1/1/01 and ending 12/31/01, prepared 3/15/02.
- Children's Tylenol Suspension (Cherry) (b) (4) Process 4 oz. Packaging Size Process Validation report # 20-VAL-PRO-C-476-3, approval date 5/4/95.
- Validation Protocol # 20-VAL-PRO-C-476-3 for (b) (4) Process Children's Tylenol Cherry Suspension Packaged in 4 oz. bottles (Manufactured Using (b) (4) and (b) (4)

- R&D Finished Product Bulk Product Stability Protocol for St. Joseph Chewable Tablets (C-932) # BPSP-46, approval date 12/14/00.

- St. Joseph Chewable Tablet Interim Bulk Hold Stability Summary and Environmental Assessment Report # BPSR-35, approval date 2/23/01.

- St. Joseph Chewable Tablet Interim Bulk Hold Stability Summary and Environmental Assessment Report (Supplement 2), approval date 6/15/01.

- Process Validation Report St. Joseph Chewable Aspirin 81 mg Tablet Formula C-932-1, Protocol # 20-VAL-PRO-30051, approval date 2/20/01.

- St. Joseph Chewable Aspirin Tablet (C-932-1) Process Validation Report # 20-VAL-PRO-0051, approval date 4/4/01.

- SOP entitled "Recall Procedure" 99-QA-QA-030, effective date 3/22/99.

- SOP entitled "Complaint Investigations" 99-QA-QA-002, effective date 6/22/99.

- SOP entitled "Nonconformance Control Procedure" 20-QA-QA-009, effective date 1/19/01.

- Effectiveness of Antimicrobial Agents in Children's Tylenol Suspension C-476-3, dated 9/10/92.

- Tylenol Suspension Products Change of Butylparaben Specification, dated 10/30/98.

- Validation Protocol # 20-VAL-PRO-C-476-3 for (b) (4) Packaging Process Using (b) (4) for Children's Tylenol Cherry Suspension Packaged in 4 oz. bottles (Manufactured Using (b) (4) (b) (4) and (b) (4) approval date 11/28/95.

- Children's Tylenol Suspension (Cherry) (b) (4) Packaging Process Using (b) (4) Hold Tanks for Children's Tylenol Cherry Suspension Packaged in 4 oz. Package size Packaging Process Validation Report # 20-VAL-PRO-C-476-3, approval date 1/11/96.

- Children's Tylenol Suspension Liquids (Cherry Flavor, C-476-3 (b) (4) Process in a (b) (4) Hold Tank Scale-up Report, approval date 1/17/96.

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- Moisture Absorption Rate Capacity of (b) (4) Desiccant Canisters Used in St. Joseph Products C-932 and C-933 Research Report # RR-930, approval date 4/26/01.

- Children's Tylenol Suspension Liquid – Cherry Flavor 160 mg/5ml Manufacturing Requisition (MR) batch #'s (b) (4) reviewed by QA on 2/22/02) and (b) (4) reviewed by QA on 12/30/01.

- Packaging Records for Tylenol Pediatric Cherry Suspension Liquid batch #'s (b) (4) (approved/released by QA on 2/26/02) and (b) (4) (approved/released by QA on 1/2/02.

- St. Joseph Chewable Aspirin Tablet Final Blending and Compression MR for batch #'s (b) (4) reviewed by QA on 11/1/01), (b) (4) (reviewed be QA on 11/1/01), and (b) (4) (reviewed by QA 3/11/02).

- Packaging Records for St. Joseph Aspirin Chewable 81 mg tablets batch #'s (b) (4) reviewed/approved by QA on 11/4/01) and (b) (4) (reviewed/approved by QA on 3/19/02).

- Cleaning Validation Protocol # 20-ECVP-0126 for the Removal of Acetaminophen from the (b) (4) Tablet Presses, approval date 6/6/01.

- Cleaning Validation Report # 20-ECVP-0126-FR for the Removal of Acetaminophen from the (b) (4) Tablet Presses, Rev. 1, approval date 8/24/01.

- Cleaning Validation Protocol # 20-ECVP-0087, Rev.1, for the (b) (4) Tank System in Liquids Processing approval date 10/6/00.

- Cleaning Validation Report # 20-ECVP-0087-FR, Rev.1, for the (b) (4) (b) (4) Tank System in Liquids Processing approval date 5/16/01.

- Validation Protocol # 20-ECVP-0086 for Cleaning the (b) (4) Delivery System, approval date 8/29/00.

- Cleaning Validation Report # 20-ECVP-0086-FR for the (b) (4) Delivery System, Rev. 1.0, approval date 7/18/01.

- McNeil Consumer Healthcare Company Johnson & Johnson Merck ERP (Enterprise Resource Planning) System SAP R/3 Validation Report

ERPV0383, Plant Maintenance Module Implementation in Version 4.5.6. VCS024, approval date 10/29/01.

- Cleaning Validation Report # 20-VP-ECVP-598, Bulk Processing and Filling Equipment Used in Manufacture of Children's Tylenol Suspension Liquid (Bubble Gum Flavor), approval date 6/29/94.

No deviations were observed except as noted in the DISCUSSION WITH MANAGEMENT Section of this report.

FIELD ALERTS/RECALLS

The following Field Alerts and/or Recalls were reviewed during this inspection:

- Field Alert for Motrin Suspension 20 mg/ml 1 oz. professional sample package batch #(b) (4) expiration date 2/01. Initial notification was submitted to FDA on 3/16/00. Final report was submitted to FDA on 5/9/00. According to Lab Investigation #(b) (4) this batch failed 12-month stability station for resuspendability. Production investigation (b) (4) was also reviewed.
- Field Alert for Motrin Suspension 20 mg/ml, Bubble Gum flavor, 4 oz. package, batch #(b) (4) expiration date 7/03. Initial notification was submitted to FDA on 10/11/00. Follow-up notification submitted to FDA on 11/9/00. According to investigation, berry flavor cartons were found within a bubble gum flavor batch. Corrective action instituted as the result of this deviation was also reviewed.
- Level III recall of Women's Tylenol Menstrual Relief Caplets 40's lot DJM099 expiration date 9/02 was initiated by the firm on 8/23/01. This product is manufactured by McNeil facility located in Guelph, Ontario, Canada and packaged into bottles by McNeil, Fort Washington. According to investigation, the batch initially failed dissolution on 30-day accelerated stability and then went to stage III dissolution on 12-month stability under the controlled room temperature conditions. Final report informing FDA about the recall completion was filled on 3/21/02.
- Field Alert for Junior Strength Children's Motrin Grape Chewable Tablets, 24 count bottle, batch #(b) (4) expiration date 2/03. Initial Field Alert was submitted to FDA on 3/1/02. According to the consumer complaint received by the firm, the bottle contained 24 Women's Tylenol Menstrual Relief Caplets. As a result of this complaint the firm has initiated a recall on 3/21/02 during this inspection.

RECALL PROCEDURES

SOP 99-QA-QA-030, entitled "Recall Procedure", effective date 3/22/99 was reviewed during this inspection. In addition, the firm was able to demonstrated lot traceability. No deviations were observed.

TRAINING

SOP 99-NQA-CC-005, entitled "Good Manufacturing Practice (cGMP) Training, effective date 6/13/00 was reviewed. According to this SOP, all new employees who are to be engaged in the manufacture, processing, packing, holding, testing and release of drug products receive a new employee cGMP orientation prior to executing a job task in Operations or QA. All Operations and QA personnel are provided with cGMP training at least once every calendar year. In addition, training on specific cGMP related topics is provided periodically. The cGMP training is usually performed by individuals who have received appropriate training through an approved trainer's program.

Ms. Boyles explained that all new employees receive the General Department training that includes training in safety, cGMP's and SOP's. There is also the Technology Specific training, which includes on-the-job and classroom training directed at the specific job function(s) that an employee will be performing.

I reviewed training records for Alicia Robinson/Liquid Packaging Line Tender, James Deloach, Liquids Packaging Operator, and William K. Witta, Compliance Specialist. Mr. Witta received the trainer's program cGMP training. He indicated that he is qualified to act as a cGMP trainer at Fort Washington facility.

No deviations were observed.

CORRECTIONS

Corrective actions instituted by the firm in response to the FDA-483 Observations from the previous inspection were reviewed. No deviations were observed.

DISSCUSIONS WITH MANAGEMENT

1) According to Nonconformance Investigation #(b) (4) approved on 2/28/02 (Exhibit 14), a small piece of foreign material was found in the finished packaged sample used for micro testing of Tylenol Pediatric Cherry Suspension Liquid, 4 oz., batch #(b) (4) It was determined to be a 1mm X 3 mm piece of inert black rubber. The probably root cause of this incident was determined to be

supplier gasket damage since the rubber material found in the sample did not match that any of gaskets or seals in the processing of the product. Although not stated in the investigation, Ms. Devine explained that the piece of rubber could not have come from the raw material because there are in-line (b) (4) mesh sieves, which would retain a foreign material of this size. Therefore, it was concluded that the contamination was possibly introduced by the manufacturer of packaging components (bottles or caps). Additional samples were taken from the batch and examined for presence of foreign material. None was observed.

Ms. Devine explained that the follow up at the packaging components suppliers is pending. I inquired whether the firm has evaluated any other batches of products that were packaged using the same lot(s) of components as batch # (b) (4) Ms. Rademacher indicated that they have not. She presented me with the list of finished product batches packaged using cap lot # (b) (4) and bottle lot # (b) (4) that were also used in packaging of Tylenol Pediatric Cherry Suspension batch # (b) (4) (Exhibit 15).

Later during the inspection Ms. Devine also presented me with a letter from (b) (4) (the supplier of 4-ounce bottles) dated 3/27/02 (Exhibit 16). This letter documents that black rubber is used in a process of bottle manufacturing. However, the review of the supplier's production records for the subject lot of bottles along with the preventive maintenance documents did not uncover any abnormal occurrences or deviations during production. In addition, the firm received a letter from (b) (4) the manufacturer of caps, dated 3/27/02 (Exhibit 17). It documents that according to the supplier's findings the black piece of rubber gasket could not have been introduced during the manufacturing of a subject lot of caps. After receiving these letters the firm inspected the retain samples from all of the batches that were packaged using the same bottles lot as batch # (b) (4) No foreign materials were found. Exhibit 18 is a copy of a follow-up investigation dated 3/28/02.

I pointed out to the firm that other batches of products that could have been affected by a deviation should always be evaluated during the Nonconformance investigation. Also I indicated that the Nonconformance investigation should contain as many details as possible about the event and a follow-up action taken as the result of this event.

2) On my review of MR for St. Joseph Chewable Tablet batch # (b) (4) (Exhibit 19), under Final-Blend processing directions, it is documented that step 13 (b) (4) (b) (4) must be completed in (b) (4) (b) (4) (b) (4) lumping stop time was originally documented as (b) (4)

(b) (4) on 3/6/02, which exceeds a time specification of (b) (4) However, dumping stop time of (b) (4) was crossed out by the operator on 3/6/02 and corrected to (b) (4)

According to Ms. Boyles, there is no Nonconformance Investigation associated with this deviation. She contacted the operator whose initials appear under step (b) (4) of MR to get an explanation of this event. She indicated that according to the operator, he recorded the dumping start time using the production room clock. However, he recorded the dumping stop time using his personal watch which where (b) (4) Another operator pointed out the deviation to him. At which point the mistake was corrected.

I pointed out to Ms. Boyles and Ms. Rademacher that this type of deviation should be captured under the firm's Nonconformance system and the reason for the correction made in MR should be documented. As the result of this incident, the firm has introduced a new procedure entitled "Good Documentation Practices". I was presented with the draft of this SOP (Exhibit 20).

The following section of the report was written by Chemist Wood.

In instrument E-FTW-VCP-001, vector coating pan for tablet coating, I observed what appeared to be white Teflon tape hanging loose underneath the second coating spray nozzle from end of the line inside the instrument. This was mentioned to Elizabeth Boyles, Solid Dose Processing Manager and investigated. Ms. Boyles later informed me that the observed material was Teflon tape and was located around gun assembly below the nozzle. It is routinely used there to prevent leakage of the coating material. In this observed instance, the end of the tape hadn't been properly cut and therefore left a "tail". There are inspections performed every (b) (4) to check the spray nozzles to ensure that no coating has collected. The tape was not noticed during prior (b) (4) check, but was removed after I mentioned it at the next (b) (4) check. Ms. Boyles mentioned that due to the tape's chemical- and heat-resistant properties, there was no threat of product contamination.

Research and Development (R&D) Laboratory:

R&D laboratory upgrading HPLC software from (b) (4) (b) (4) Installation, operation and performance qualifications have been completed; analysts are currently going through training and regular use of the software. (b) (4) software has been retained to retrieve data from that system.

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In room RC232 HPLC instrument 6 was observed; consists of (b) (4) controller, (b) (4) autosampler and (b) (4) detector. This instrument is calibrated every (b) (4) The maintenance log was reviewed.

In rooms **RC229 and RC228**: observed (b) (4) Automatic Polarimeter. This is a new instrument and is still in Installation, Operational and Performance Qualification (IQ/OQ/PQ) stage. Observed HPLC instrument 56 in use. Instrument consists of (b) (4) autosampler, (b) (4) pump, (b) (4) dual wavelength detector and (b) (4) Refractive Index (RI) detector. This HPLC is calibrated by outside contractor every (b) (4) and internally for small changes or repairs in the interim.

A (b) (4) analytical balance, instrument (b) (4) was observed flashing a "CAL" symbol on the readout display. The logbook (E96-24) was reviewed. I spoke with Ms. Carmela Walter, Research Scientist – Research & Development, about the flashing "CAL" and mentioned that this means the balance is waiting for an internal calibration to be performed. This issue was raised at the previous inspection as well. SOP 99-RD-IN-003, "Analytical Balance Calibration and Testing" (Exhibit 21), specifies external weight checks (b) (4) with (b) (4) different weights and internal calibration of instrument only when one of these weight checks doesn't meet requirements. I spoke with Ms. Carmela Walter and was told that they spoke with a representative from Mettler Toledo when this issue was raised during the last inspection and was told that the internal mechanism of the analytical balance was delicate and performing too many internal calibrations can cause problems. I contacted a representative from (b) (4) he evening of March 26th 2002 and was told that the flashing "CAL" signal is automatically lit every (b) (4) (b) (4) and when the balance senses a (b) (4) change in temperature in the environment. This function can be turned off. Ms. Walter was told the same thing when she called (b) (4) that same evening. I asked what should be done as a minimum as far as calibrating or checking the balance is concerned. Sophia said that either an internal calibration or an external weight check should be performed at least (b) (4) This is also typical industry practice. The SOP has been updated, effective date 04/11/2002, to reflect an external weight calibration check each day of use (Exhibit 22).

The (b) (4) melting point apparatus was observed. (b) (4) a new instrument, is still in IQ/OQ/PQ process.

Room **RC230**: observed (b) (4) which was previously used for (b) (4) research. It was moved to this location 4/2001 and is still awaiting PQ process. Associated logbook E-022 was reviewed.

(b) (4) was observed and associated logbook E-156 was reviewed.

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(b) (4) Laser Scattering Particle Size Distribution Analyzer was observed. Logbook E-181 showed that this instrumentation was received in 12/2001.

(b) (4) Laser Scattering Particle Size Distribution Analyzer was observed. Logbook E93-033 was reviewed.

Upon viewing (b) (4) instruments, I noticed that one was designated "USP only" and one was designated "USP/JP". I asked what this meant and was told that some of the (b) (4) are qualified to meet only USP requirements and others are qualified for using USP and / or JP methodology.

End Chemist Wood.

ANALYST REPORT

The following section was written by Chemist Wood.

Company changes:

Former Vice President of Marketing became President of company, William McComb

Name change of company from McNeil Consumer Healthcare

Quality Assurance and Compliance is now Quality Services and Compliance

Pre-Approval Inspection: Loratadine tablets, 10 mg

Stability testing for clinical batches of this product is performed at Fort Washington site.

Stability testing for the marketed product is performed at the Lancaster, PA J&J / Merck facility.

Caraustar (Clifton, NJ) packages Loratadine tablets in pouches.

GMP Inspection:

New liquids manufacturing area at the Fort Washington site (Liquids Manufacturing Area #1) is in development stage and should be fully functional by next year. This area has undergone installation, operation and performance qualifications for equipment and computer systems. The existing liquids manufacturing area (Liquids Manufacturing Area #2) and the new liquids manufacturing areas will be run together for estimated 12 – 18 months until after all application approvals have been completed. Per Larwrence Constable, Plant Manager, there are no set plans for the existing liquids manufacturing area after its closure.

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Children's Tylenol Suspension – Cherry Flavor

Investigation number (INV #)(b) (4) Batch # (b) (4)
Out-Of-Specification (OOS) Result occurred: 10-13-00
Investigation concluded: 10/16/00
After investigation, the OOS result was attributed to the analyst. There was a shaking error during the final dilution step of sample preparation. Associated batches and suspect batch were all retested and were within specifications.

INV #(b) (4) Batch #(b) (4)
OOS Result occurred: 2/3/01 Investigation concluded: 2/6/01
Retesting (re-injecting with a fresh vial) supported the OOS result since system suitability and control samples were acceptable. The analyst re-sampled from the suspect bottle and a control sample. The new results were acceptable. The OOS was attributed to sample preparation error by analyst. The associated batches were also re-prepared and all values replaced since the sample preparation error could not be guaranteed to be isolated to only the suspect sample.

INV #(b) (4) Batch #(b) (4)
OOS Result occurred: 1-22-02 Investigation concluded: 1-23-02
The middle of the batch had a high, OOS assay result. The system suitability and other batches were acceptable. Retest showed control confirmation, but not OOS confirmation. The OOS result was attributed to sample preparation error by the analyst. All associated batches were re-sampled since the sample preparation error could not be guaranteed to be isolated to only the suspect sample.

INV (b) (4) Batch #s(b) (4)
(This investigation also included Infant's Tylenol Suspension – Grape Batch (b) (4)
OOS Result occurred: 1-23-02 Investigation concluded: 1-23-02
All (b) (4) atches (and a stability sample) were OOS with high assay results. The investigation revealed a standard preparation dilution error by the analyst; the OOS results were attributed to this analyst error. All of the batches were retested (re-injected) with a new standard preparation and were within specifications.

INV #(b) (4) Batch #s(b) (4)
(b) (4)
OOS Result occurred: 1-29-00 Investigation concluded: 2-9-00
DAM111 – beginning and middle of batch were OOS with low assay results; end of batch and bulk batch assays were out-of-trend (OOT) but within specifications

(b) (4) beginning, middle, end and bulk batch assays were OOT but within specifications.
Re-injection of vials confirmed OOS; the sample final dilution solution was remixed and re-measured and also confirmed OOS results. Associated Non-Conformance Report (NCR) (b) (4) went into further detail about suspected root cause of the OOS: a weighing problem in the Chemistry Weighing (Chem Weigh) area when the skid weight was inadvertently added to the actual product weight instead of being tared to zero. Corrective action included addition of specific tare weight information to the chem. weigh batch cards to better keep track of the weighings. All lots were destroyed after investigation.

St. Joseph Orange Chewable Tablets

INV #: (b) (4) Batch #s: (b) (4)
OOS Result occurred: 5-3-01 Investigation concluded: 5-4-01
Content uniformity (CU) tests were OOS with high results for two vials per batch. Retesting showed no confirmation for these samples but confirmed the control. These OOS results were attributed to equipment error (air lines in the HPLC system) and all batches were run again for replacement results.

INV #: (b) (4) Batch #: (b) (4)
OOS Results occurred: 6/27/01 Investigation concluded: 6/29/01
The aspirin assay result was OOS high. A standard investigation was performed per SOP 99-QA-LP-047 "Laboratory Investigations and Retest Procedures" to ensure proper standard preparation. The standard was found to be suitable. During analysis, the method was started and system suitability was not met. The method was ended and restarted and the same vials were analyzed. The investigation concluded that the vials which had already been punctured underwent concentration of analyte due to evaporation of the diluent (approximately (b) (4) - a volatile solvent). Sample vials were re-poured and analyzed with suitable results.

Materials Reviewed:

Log book E96-19 for stability chamber identified "JV Chamber #7".
Stability data for (b) (4) Viewed dissolution and assay data for initial testing, one month, two months, three months and six month accelerated testing (b) (4) of batches (b) (4) (b) (4) Viewed dissolution and assay data for nine month testing (b) (4) for batches (b) (4)
Notebook reference NB 671: 120-127 which contains raw data for one month dissolution testing of batch (b) (4)

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"Report of the Transfer of the Analytical Method for the Assay of (b) (4) Method No. 1084FP version 3.2 (07/20/00) From (b) (4) to McNeil Consumer Healthcare R & D Laboratories and (b) (4) (b) (4) Method Lab Transfer Report #AMLT-775. This document includes the correlation of data between (b) (4) McNeil and (b) (4) analysts (b) (4) analysts are internally contracted to McNeil. The transfer is considered to be successful according to (b) (4) protocol, quoting (b) (4) SOP C-10-100-01-00 "Transfer of Analytical Methods to Quality Control" dated June 12, 1997.

Instrument logbook E-119 for (b) (4) instrument #61 in R&D laboratory, room RC232. This HPLC system consists of a (b) (4) pump, a (b) (4) autosampler (b) (4) and a (b) (4) detector and was used during analysis of (b) (4) tablets.

Instrument logbook E-120 for (b) (4) HPLC instrument #62 in R&D laboratory, room RC232. This HPLC system consists of a (b) (4) pump, a (b) (4) autosampler (b) (4) controller (b) and a (b) (4) detector (b) (4) and was used during analysis of (b) (4)

Training record of employee Brian Hill, Stability Manager. Mr. Hill is a contract employee through (b) (4) whose primary duties involve monitoring the (b) (4) system and responding to alarms. The (b) (4) system controls and maintains the stability chambers.

SOP 99-RD-AN-030 "Finished Packaged Product Developmental Stability Procedures", effective 01/05/2001, which outlines steps for collecting stability samples for analysis.

SOP 99-QA-LP-047 "Laboratory Investigations and Retest Procedures", effective 02/04/2000, which establishes the procedure for investigating any analytical laboratory result that doesn't comply with approved specifications, expected trends or are otherwise questionable scientifically.

Report of Annual Product Review Approvals for St. Joseph Chewable Tablet, Orange Flavor (b) (4) for the review period 2/1/01 – 1/31/02. From this report, the following marketed bulk batches were selected to review a portion of the raw data (b) (4) (content uniformity, aspirin assay and dissolution), (b) (4) content uniformity and aspirin assay), (b) (4) (content uniformity and aspirin assay) and (b) (4) (dissolution).

Report of Annual Product Review Approvals for Children's Tylenol Suspension, Cherry Flavor (b) (4) for the review period 1/1/00 – 12/31/00. From this report, marketed product batch (b) (4) was selected to review aspirin assay results and butylparaben assay results. This report includes reference to (b) (4) which resulted in the destruction of product batches (b) (4) and (b) (4)

SOP 20-QA-LP-029 "Marketed Product Stability Samples", effective 11/02/2001, which establishes process to acquire stability samples of marketed products.

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Research report #(b) (4) Interim Bulk Hold Stability Summary and Environmental Assessment Report" for St. Joseph Chewable Tablets. The following records for product batch (b) (4) were reviewed: dissolution values for top and middle samples of tote bin at one month (b) (4) (b) (4) conditions) which passed at (b) (4) ssolution testing (reference NB (b) (4) dissolution testing for three months (b) (4) conditions after exposure to (b) (4) conditions for (b) (4) which passed at (b) (4) testing (reference NB (b) (4) (b) (4)

"Working Reference Standards Log" maintained by R&D laboratory which is a written log of which standards are issued, where they're sent, expiration date and return status after expiration.

SOP 99-RD-AN-003 "Reference Standards", effective 10/19/2000, which details how USP/NF (or equivalent pharmacopeial standards) are used to certify working standards which are then issued to various laboratories. Also describes testing requirements, expiration dating, procurement, storage and dispensing of working reference standards.

For St. Joseph Chewable Tablet, Orange Flavor, reviewed data for marketed product stability batch (b) (4) This data included initial (release), three month (actually four month – timepoint was missed), six month and nine month testing. There were no OOS results associated with the stability testing of this batch.

For St. Joseph Chewable Tablet, Orange Flavor, reviewed raw data for marketed product stability batch (b) (4) The data for initial, four month, six month and nine month testing was reviewed. Non-conformance report (NCR) (b) (4) was associated with batches (b) (4) These batches were originally packaged without dessicant in the bottle to prevent moisture absorption. Based on the stability testing at six month timepoint, the data showed that dessicant is not needed and these batches were released.

For St. Joseph Chewable Tablet, Orange Flavor, reviewed raw data for marketed product stability batch (b) (4) Initial, three month, six month and nine month data reviewed. This batch was packaged with dessicant. Some test values were slightly higher, but within specifications.

For Children's Tylenol Suspension Liquid marketed batch (b) (4) manufacture date 950409, I reviewed stability data for initial, three month, six month, nine month, 12 month and 24 month testing. The study was begun in 4/95 in the QC laboratory and transferred to R&D laboratory (along with all other stability responsibilities at this facility) where it was completed. Stability responsibilities were transferred back to QC laboratory circa early 1998. There was a suspect result at the 24 month timepoint for another batch with which (b) (4) was associated. The root cause of the suspect was determined to be a mixing error by analyst. The sample was re-prepared and retested.

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For Children's Tylenol Suspension Liquid marketed batch (b) (4) I reviewed stability data for initial, three month, six month, nine month, 12 month and 24 month testing. This batch was associated with the same batch as (b) (4) for the 24 month suspect result.

For Children's Tylenol Suspension Liquid marketed batch (b) (4) I reviewed stability data for initial, three month, six month, nine month, 12 month, 18 month and 24 month testing. This study began 1-31-00 and was concluded 1-2002.

For Children's Tylenol Suspension Liquid marketed batch (b) (4) I reviewed stability data for initial, three month, six month, nine month and 12 month testing. The initial testing was awaiting microbiological results when the three month stability testing was started, but all timepoints were hit on time.

SOP 20-QA-IPAP-019 "Balance Calibration and Daily Check Procedure", effective 11/30/2001, details six month calibration by outside contractor; daily balance check each day of use; and when internal calibrations are performed.

SOP 20-QA-IPAP-023 "Laboratory Balance Calibration", effective 11/28/2001, specifies calibration activities performed by the outside contractor every six months. Internal personnel do not perform this testing. The procedure was provided by the contractor and incorporated into Fort Washington's SOP system.

Analytical results for Children's Tylenol Suspension – Cherry Flavor: marketed batches (b) (4) bulk batches (b) (4) (b) (4)

"Report on the Method Linearity of ACV-040 [analytical cleaning validation] and the Cleaning Validation Recovery of Acetaminophen from (b) (4) Stainless Steel Using New Swabbing Technique – Revision 2", which is the report used to evaluate the cleaning of the (b) (4) Tablet Press and validate the cleaning protocol. The linearity and feasibility studies were performed onsite, while the majority of the swab recovery testing was performed by (b) (4) (b) (4) However, the (b) (4) swab recovery" value reported in the method was generated onsite during the feasibility study as it was the worst case scenario of all of the studies performed. I reviewed the raw data for (b) (4) testing of Acetaminophen and cleaning agent (b) (4) Method ACV040 "Cleaning Validation Procedure Acetaminophen", effective 001117, used for swabs, solutions and cloths as needed. Method ACV-043 "Cleaning Validation Procedure (b) (4) effective 010514, used for swabs, solutions and cloths as needed.

Analytical results for St. Joseph Chewable Tablet Orange Flavor, bulk batches (b) (4) and marketed batch (b) (4) both bulk batches were used for this marketed batch).

Analytical results for St. Joseph Chewable Tablet Orange Flavor, marketed batch (b) (4) and bulk batch (b) (4)

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St. Joseph Chewable Tablet Blend Bulk Hold Stability Summary and Environmental Assessment Report, Research Report #: (b) (4) (also Supplement 1, Revision 1: (b) (4)) which supports the (b) (4) hold time in a (b) (4) holding bin between blending and compression of a batch. The study reported testing performed on blend batch (b) (4) which was held for (b) (4) and then compressed, packaged and placed on three month accelerated stability testing (b) (4) After (b) (4) months, results for assay, dissolution and salicylic acid tests were still within specifications.

Quality Control (QC) Laboratory:

QC laboratory is in the process of upgrading from (b) (4) to (b) (4) software. This software will begin to be utilized on / about April 15th and staggering setup over approximately a (b) (4) period. This upgrade is expected to correct a current issue with chromatographic data; namely, chromatograms are lost after approximately (b) (4) and are irretrievable. The only copy of the data at that point is the paper copy generated by the analyst after the run is completed.

(b) (4) Spectrometer (b) (4), instrument (b) (4) was observed. Logbook #2 and maintenance log were each reviewed. Instrument is calibrated every (b) (4) (b) (4) instrument (b) (4) was observed. Logbook and maintenance log reviewed.

Balances are calibrated every (b) (4) by outside contractor and daily check by analysts includes external check with (b) (4) weights (depending on model) but no internal calibration unless (b) of the weight checks fails. Applicable SOPs reviewed: 20-QA-IPAP-023 "Laboratory Balance Calibration", effective 11/28/2001 and 20-QA-IPAP-019 "Balance Calibration and Daily Check Procedure", effective 11/30/2001.

(b) (4) dissolution apparatus, instrument (b) (4) was observed. Dissolution apparatuses are calibrated every (b) (4) Reviewed logbook and maintenance log.

I questioned Robert Hausel, QC Laboratory Team Leader, about Reference Standards in the QC laboratory and was informed that: USP standards are replaced when they expire (as per USP catalog) and working reference standards (WRSs) are recertified annually and are tracked in logbooks at each standard location and by R&D. Additionally, the analysts are responsible for checking a standard's expiration date before use.

(b) (4) Particle Size Distribution Analyzer (b) (4) instrument (b) (4) was observed. This instrument is calibrated every (b) (4) (b) (4) The logbook and maintenance log were reviewed.

Gas chromatograph (b) (4) instrument (b) (4) was observed. This instrument hasn't been used for analysis since 11/99. There was a "Do Not Use" notice dated 11/00 observed on the instrument. This GC was modified for use in 10/2001 and is still being qualified. The logbook and maintenance log were reviewed.

High Pressure Liquid Chromatograph (HPLC) system (b) (4) instrument (b) (4) was observed. There was a notice on the instrument that pump B is leaking dated 3-25-02. The system is still acceptable to use for isocratic runs which do not require pump B to be active.

(b) (4) viscometer, instrument (b) (4) was observed. This instrument is calibrated every (b) (4) using certified (b) (4) oils.

(b) (4) Melting Point Apparatus, instrument (b) (4) was observed. The instrument is calibrated every (b) (4) Review of logbook corroborated the use of this instrument by personnel in the R&D laboratory during the period that R&D melting point apparatus was not working (see follow-up to previous 483, observation #11).

Computer Systems

Per discussion with Mr. Craig McDonald, Senior Analyst, there are (b) (4) levels of username / password combinations required to enter the Laboratory Information Management System (LIMS). LIMS is used for tracking samples (including samples receipt, analysis results, approval), report generation, audit trail for sample changes and certificates of analysis. There has been no purging of data from the system since it's inception in 1993. SOP 99-QA-LIM-006 "LIMS Sample Modification", effective 03/28/1997 (currently in "In Review" status to be updated), covers adding / removing tests, deleting optional tests, changing number of test replicates, changing sample header, test results copy, viewing sample audit trails and / or purging samples from LIMS. Samples are not often purged, but this may be performed to delete validation tests that are deemed unnecessary or temporary samples assigned during PQ of LIMS. There are (b) (4) different user security levels within LIMS that permit different operations ranging from basic sample log-in to system manager status and the user level determines what kinds of changes can be made.

I reviewed SOP 20-IM-LIM-003 "Backup for LIMS Systems", effective 01/29/2001, which describes the procedure and schedule for performing tape backups for LIMS. Per discussion with Mr. John Humble, Senior Information Management Consultant, when backup tapes are completed they are stored in a secure vault in the Data Center onsite which is accessible only to analysts in Computer Operations. SOP 20-IM-OPS-062 "Off-Site Media Circulation Procedures", effective 01/03/2002, describes the rotation and retention of backup media to and from the McNeil Fort Washington facility and the off-site media vendor. Daily backups and

weekly backups are performed, kept on site for no more than (b) (4) and are sent off-site where there are stored for (b) (4) and then returned to the media pool ("rotation"). (b) (4) backups are stored offsite for (b) (4) backups are stored offsite for (b) (4) QA / chromatography back-ups do not include raw data files, only the software associated with HPLCs.

SOP 20-IM-LIM-004 "Restoring Files from LIMS Backup", effective 01/29/2001, defines the steps for requesting file restoration and associated documentation.

Training

SOP 99-QA-LP-043 "Laboratory Training Program", effective 02/12/2002, which describes general training requirements for all analysts (including chemists, technicians, inspectors) in all McNeil QA laboratories. Some specifications regarding training include: qualified trainer; training must be documented; training data will be reviewed and approved by trainer and supervisor; training will be sufficient to ensure that trainee can perform the task with minimal supervision; training data will be retained as long as the employee holds analyst position and archived for (b) (4) thereafter. Training defined as mandatory in this SOP includes: cGMPs, Good Laboratory Practices, SOPs, USP, laboratory systems, product specifications and analytical methods.

SOP 20-QA-LP-034 "Training Requirements for QC Analytical Lab Personnel", "In Review" status, incorporates 99-QA-LP-043 with extensive listing of in-house training requirements and checklist for different analytical areas and sampling / inspection. Covers areas including: dosage forms, raw materials, USP training and calibrations. Additional note: SOPs with a (b) (4) designation indicates a (b) (4) procedure while a (b) (4) designation indicates a national (b) (4) procedure..

Training folder of Kristina Haines was reviewed. Ms. Haines entered on duty as an official McNeil employee on 04/16/2001. Ms. Haines was originally contracted through (b) (4) to McNeil in 2000. Issues reviewed in her "Corrective Action" folder: 11/01 - use of Assay HPLC multimethod instead of appropriate Dissolution Rate multimethod; 6/01 – HPLC system suitability not met; new standard vials re-poured but no new assay vials poured initially upon restart; 11-4-00 – pipetting error during sample preparation; 11-2-00 – incorrect cell size used for UV dissolution analysis.

Raw Material OOS investigations

NC # (b) (4) Product: High Fructose Corn Syrup (HFCS) 55%
Lot # (b) (4)
Report created: 3-11-02

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Color test result of (b) (4) failed to meet specification of (b) (4) The root cause of this nonconformance was determined to be product overheating by (b) (4) before receipt at Fort Washington facility. Material was returned to (b) (4) for credit issuance. This nonconformance report is associated with laboratory INV (b) (4)

NC # (b) (4) Product: Xanthan Gum NF
Lot # (b) (4)
Report created: 10/01/2001
Viscosity test result of (b) (4) failed to meet specification of (b) (4) Supplier test on certificate of analysis met specifications; however, when the product was returned to supplier for testing, their results confirmed the McNeil results. The investigation into this matter later revealed that the instrumentation at the supplier was faulty when the certification analysis was performed. This nonconformance report is associated with laboratory INV # (b) (4) which is the investigation of OOS and the ultimate rejection of this lot.

NC # (b) (4) Product: HFCS 55%
Lot # (b) (4) and (b) (4) associated batches (b) (4) bulk batches and (b) (4) finished product batches)
Report created: 11-14-2001
During microbiological testing, an objectionable microorganism was detected. The probable root cause was determined to be contamination during transfer and sampling of the lot at the Fort Washington site. All lots were destroyed. The disposition was approved by the QA lab on 02/07/2002. It was noted in the report that the investigation exceeded the prescribed (b) (4) because of the difficulty in isolating a root cause.

NC # (b) (4) Product: MCC, NF (Avicel RC591)
Lot # (b) (4) and (b) (4) ssociated batches
Report created: 04/20/2001 Concluded: 04/26/2001
A piece of cardboard was discovered floating in a mixing tank after the addition of (b) (4) The root cause was determined to be an inadvertent addition of cardboard during repackaging process at supplier.

Follow-ups to previous 483:

Item # 11 – Per Carmela Walter, Research Scientist Research and Development, the (b) (4) Digital Melting Point Apparatus was evaluated and found to be unfit for their use in the R&D laboratory. The melting point apparatus in QC laboratory was used when needed until a new melting point apparatus was obtained for R&D. This fact was verified during my walk-through

of the QC laboratory when I noted in the melting point logbook that personnel from R&D had used that instrument. A (b) (4) Melting Point Apparatus has been obtained, calibrated and put into use as of 7/2/01.

Item #12 – SOP "99-RD-IN-006 High Pressure Liquid Chromatography Systems", effective 12/20/2001, includes wavelength accuracy test with (b) (4) and (b) (4) (checking (b) (4) wavelengths instead of one as previously noted). This was added into the contract with (b) (4) who performs preventative maintenance every (b) (4) If additional calibration is needed, it is performed in-house.

End Chemist Wood.

ATTACHMENTS

1. Assignment from PHI-DO PAI Manager;
2. FDA-482, Notice of Inspection, dated 3/20/02;
3. FDA-482, Notice of Inspection, dated 3/20/02.

EXHIBITS

1. Product list (2 pages);
2. J&J and McNeil, Fort Washington, Organizational Charts (15 pages);
3. Selected pages from SOP 20-QA-QA-007 entitled "Change Control, Issuance and Maintenance of Master Manufacturing Requisitions and Batch Records at Fort Washington, effective date 8/18/00 (4 pages);
4. Floor plan diagram, manufacturing areas 1st floor (1 page);
5. Floor plan diagram, manufacturing areas 2nd floor (1 page);
6. Floor plan diagram, manufacturing areas 3rd floor (1 page);
7. Fort Washington Facilities Upgrades (1 page);
8. Liquids Manufacturing Facility Area # 1 – Project Timeline (1 page);
9. Equipment train in a new liquids processing area (1 page);
10. Process flow diagram for St. Joseph Chewable Tablets (2 pages);
11. List of equipment used in production of St. Joseph's Chewable Tablets (2 pages);
12. Process flow diagram for Children's Tylenol Cherry Suspension (2 pages);
13. List of equipment used in production of Children's Tylenol Cherry Suspension (1 page);
14. Nonconformance Investigation # (b) (4) approved on 2/28/02 (8 pages);
15. List of batches packaged using caps lot # (b) (4) and bottles lot # (b) (4) (2 pages);
16. Supplier Awareness Training – Preventative Action memo with letter from the supplier of bottles attached (2 pages);

17. Supplier Awareness Training – Preventative Action memo with letter from the supplier of caps attached (2 pages);
18. Follow-up Nonconformance Investigation # (b) (4) approved on 3/28/02 (4 pages);
19. Selected pages from St. Joseph Chewable Aspirin Tablet Final Blending and Compression Manufacturing Requisition, batch # (b) (4) (4 pages);
20. Draft SOP entitled "Good Documentation Practices" (3 pages);
21. SOP 99-RD-IN-003 "Analytical Balance Calibration and Testing", effective date 1/30/01 (3 pages);
22. SOP 99-RD-IN-003 "Analytical Balance Calibration and Testing", effective date 4/11/02 (3 pages).

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PHI-DO, Montgomeryville RP

Yvonne C. Wood, Pharmaceutical
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