DEPARTMENT OF HEALTH AND HUMAN SERVICES

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STATEMENT OF

JOSHUA M. SHARFSTEIN, M.D.

PRINCIPAL DEPUTY COMMISSIONER

U.S. FOOD AND DRUG ADMINISTRATION

DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

COMMITTEE ON OVERSIGHT AND GOVERNMENT REFORM

U.S. HOUSE OF REPERSENTATIVES

HEARING ON

"JOHNSON & JOHNSON'S RECALL OF CHILDREN'S TYLENOL AND OTHER CHILDREN'S MEDICINES"

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RELEASE ON UPON DELIVERY

Introduction

Mr. Chairman and Members of the Committee, I am Joshua M. Sharfstein, M.D., Principal Deputy Commissioner, U.S. Food and Drug Administration (FDA or the Agency), which is an Agency of the Department of Health and Human Services. Thank you for the opportunity to discuss the Agency's regulation of drug manufacturing, our oversight of McNeil Consumer Healthcare, LLC (McNeil), and lessons learned from the ongoing investigation into quality concerns at McNeil.

FDA Oversight of Drug Manufacturing

Under the Federal Food, Drug, and Cosmetic Act, FDA is charged with, among other things, ensuring that drugs marketed in the United States are safe and effective, and are manufactured in accordance with current Good Manufacturing Practice (cGMP).

The cGMP regulations for drugs contain minimum requirements for the methods, facilities, and controls used in manufacturing, processing, and packing of a drug product. The regulations are intended to ensure purity, potency, and quality of drug products, and to prevent unsafe products from reaching consumers.

Under the cGMP regulations, each manufacturer sets specifications for its own products for such factors as potency, stability and purity, and puts in place a quality system that

ensures those specifications are met. Critical to the cGMP process is that a company must meet its own standards.

A violation of cGMP does not necessarily mean that a product is hazardous to the public. It does indicate, however, a breakdown in a manufacturer's quality system and is an indication that a company needs to take effective steps to fix the problem promptly.

FDA inspects facilities to ensure compliance with cGMP standards. These inspections occur on average for domestic facilities every two to three years. We increase the frequency of inspections for facilities when warranted by past problems or by products that are difficult to manufacture or are especially high risk.

When on site, FDA inspectors identify gaps in manufacturing standards and discuss with companies how they can fix them. Firms may choose to recall products when there are cGMP violations, especially when those violations have a significant impact on product quality or safety.

For drugs, patterns of non-compliance or non-compliance that put the public's health at risk leads to appropriate enforcement action by the Agency, including warning letters, seizures, injunctions and criminal prosecution.

Oversight of McNeil Consumer Healthcare, LLC (McNeil)

McNeil makes a variety of over-the-counter (OTC) products for the U.S. market from four manufacturing facilities in the United States and Canada. Over the last several years, FDA has had growing concerns about the quality of the company's manufacturing process. These concerns have led to a number of unsatisfactory inspections and consumer recalls. FDA has inspected the company's facilities with an increased frequency, and in February 2010, the Agency took the extraordinary step of convening a meeting with the management of the parent company, Johnson & Johnson, to express concern about a pattern of non-compliance.

Prior to 2009. Before 2009, FDA investigators identified several problems with cGMP compliance at facilities run by McNeil. These problems included laboratory controls, equipment cleaning processes, and a failure to investigate identified problems. The company generally fixed the specific problems, and the Agency inspected the firm regularly.

Spring/Summer 2009. At its Fort Washington facility, McNeil makes a wide variety of OTC products, including a large number of OTC liquid products for children.

In May and June 2009, FDA identified several cGMP violations, including McNeil's failure to meet its own standard for quality in one of the ingredients in OTC liquids.

McNeil's standard for this ingredient, known as microcrystalline cellulose, required that there be no gram negative bacteria. McNeil purchased the cellulose in partial lots that had not tested positive for this objectionable bacteria. The vendor tested other partial lots from the same large master lot and found a certain gram negative bacteria called *B. cepacia*. According to cGMP standards, McNeil should not have used any partial lots from this master lot.

In reviewing the situation, FDA scientists concluded that the risk to the public was remote. All of the drums used tested negative for the bacteria *B. cepacia*, all of the final product tested negative, and FDA agreed with the company's assessment that this bacteria would be very unlikely to grow in the final product.

Yet, because the company had not kept to its standard, it represented a cGMP violation, and the company initiated a recall of almost eight million bottles of finished product in August 2009.

Fall 2009. At its Las Piedras, Puerto Rico, facility, McNeil makes a large number of OTC pills for the U.S. market.

In the fall of last year, FDA became aware that McNeil had received reports of products from this facility having a musty odor. Yet, McNeil had not fully investigated these

reports for about a year and did not notify FDA despite the requirement that such reports be referred to the Agency within three days.

FDA inspectors urged McNeil to conduct a complete investigation, which eventually identified the source of the odor to be a chemical, called 2,4,6-Tribromoanisole or TBA, which was in the air because of a pesticide used on the wood of the pallets used to store empty medication bottles. McNeil initiated a series of recalls as the scope of the problem became clear.

The risk posed to the public by this problem included potential temporary, non-serious gastrointestinal reactions – including nausea, stomach pain, vomiting, or diarrhea. Very little is known about the chemical TBA, but in the small quantities transferred to the products, it is not thought to pose a serious risk for long-term health problems.

On January 15, 2010, FDA issued a warning letter to McNeil expressing serious concerns about the company's control over the quality of its drugs and the company's failure to aggressively investigate and correct quality problems. This letter identified significant violations of the cGMP regulations. FDA noted that neither upper management at Johnson & Johnson nor at McNeil assured timely investigation and resolution of the issues.

January and February 2010. In early 2010, FDA conducted focused inspections of McNeil at both the Las Piedras and Fort Washington facilities to follow up on a reported

problem. The report identified a 6-year-old child who died. Prior to his death, the child had been given several products manufactured by McNeil at these facilities. FDA tested the products the child had taken for potential contamination, and all results were negative. Based on the results of the testing and the results of the inspection, FDA did not find evidence to link the products to the child's death.

February 2010. On February 19, 2010, senior compliance staff from FDA's Center for Drug Evaluation and Research and from FDA's field organization met with senior officials from McNeil and its parent company, Johnson & Johnson. Attendees included the President of McNeil, the Company Group Chairman for OTC at Johnson & Johnson, as well as a number of Quality Assurance executives from both companies.

This was an extraordinary meeting. FDA requested that senior officials from Johnson & Johnson attend the meeting so they would be on notice regarding FDA's rising concerns about whether McNeil's corporate culture supported a robust quality system to ensure the purity, potency and safety of its products. FDA also raised concerns about Johnson & Johnson's oversight of McNeil due to recent multiple recalls of McNeil products and recent warning letters FDA had issued to both McNeil and its parent company, Johnson & Johnson. Based on the Fort Washington and Las Piedras inspections in 2009 as well as the firm's recent compliance history, FDA expressed its significant concern that there was a pattern of conduct including failure to report material information to FDA in a timely manner, miscalculating and/or misstating risks and benefits of their products, and reactive vs. proactive approaches to product quality problems. FDA told the company's

leadership that significant, immediate steps were needed to address issues of compliance and quality, especially in investigating product quality issues so that the company could take preventive action to avoid problems.

The Agency learned that McNeil was taking several major steps to address these issues, including implementing management reporting structure changes, hiring new managers, and engaging a third party manufacturing consultant. FDA indicated that it would continue to monitor closely and consider further action, and that it was concerned about whether the company's corporate culture was appropriately focused on product quality issues.

April 2010. In April, FDA inspectors returned to McNeil's Fort Washington facility. This inspection was scheduled sooner than usual due to McNeil's recent history of compliance problems, including numerous recalls and cGMP deficiencies discovered in the June 2009 Fort Washington inspection, which had a significant impact on the scheduling of the April 2010 inspection.

Days before the inspectors arrived, McNeil shut down manufacturing because of manufacturing issues, including particulates found in a number of liquid medications. These particulates included acetaminophen, cellulose, nickel, and chromium. FDA inspectors identified a range of cGMP violations. These included the company failing to meet its own specifications for bacteria and particulates and, for one Tylenol product, the possibility of higher than expected concentrations of Tylenol per dropper.

In reviewing the situation, FDA scientists concluded that the risk posed to the public by these problems was remote. FDA did not find evidence that McNeil used raw materials that its tests found to be positive for bacterial contamination and all lots of finished product were tested by McNeil and found negative for bacterial contamination. The particulates would be expected to pass through the gastrointestinal tract. While there was a potential for higher concentrations of Tylenol per dropper, none of the final products released for sale tested with high levels. In addition, the increase in potency would not be expected to cause adverse effects.

Although the public health risk from these quality problems is low, these problems should never have occurred, and the cGMP failures at the facility that caused them were unacceptable. Following cGMP requirements assures that products are consistent in their safety and effectiveness and failure to follow those procedures undermines consumer confidence. On April 30, 2010, McNeil announced a voluntary recall of over 136 million bottles of liquid infants' and children's products.

Next Steps in FDA Oversight of McNeil

Based on the pattern of concerns found at McNeil's facilities, FDA is working with the company to address its systemic quality issues. The Agency is closely monitoring the implementation of a corrective action plan developed by McNeil that includes significant

enhancements to its quality system, organizational changes, and senior management oversight.

FDA will continue to investigate issues related to the Fort Washington facility including oversight related to renewal of manufacturing operations at that facility, to evaluate the facility's suppliers, and evaluate the compliance of all other McNeil facilities. FDA will also take steps to help ensure that when the facility begins manufacturing again it will be able to produce safe products. FDA is also considering additional enforcement actions against the company for its pattern of non-compliance which may include seizure, injunction or criminal penalties.

Adverse Event Evaluation

It is understandable that many Americans, hearing about these large recalls, would wonder whether or not their children were put at risk. In assessing this question, FDA considers two basic sources of information – first, our assessment of the manufacturing problems themselves, and second, adverse event reports to the Agency.

As I discussed earlier, FDA analyzed the various manufacturing problems. Based on the circumstances in each case, our experts believe the risk for any child in the United States was remote.

FDA has also looked at adverse events reported to the Agency. FDA receives these reports and often requests and reviews medical records, coroner's reports, and other supplementary data sources.

When we have adequate information about a case, the Agency reviews these reports to determine what role, if any, the medication played in the development of an adverse event. We can find that the medication likely had no role in the adverse event, that the medication's activity as a drug could have caused a serious side effect, or that a quality problem may have contributed to the outcome.

All drugs have side effects, and some of the McNeil reports may reflect the side effects of OTC medications. Other reports appear unrelated to the medications.

So far, FDA has no cases with evidence that a product quality issue contributed to a significant adverse health outcome. We are continuing to receive information about certain cases and we will update the public and the Committee should our assessment change.

Lessons Learned

Every investigation presents an opportunity for FDA to improve our effectiveness in protecting the public health. One lesson to be drawn from the McNeil story is that it is important for the Agency to even more fully consider the corporate structure when

investigating and enforcing the law. FDA will be developing new procedures to use what we learn at one facility in guiding our inspections of other facilities run by the same company.

FDA is also using these events as part of an ongoing review of our recall process. FDA has already made significant changes to its approach to recalls when there are urgent, life-threatening product quality concerns. For example, in recent months, FDA has moved aggressively to support several urgent food recalls. FDA is now looking at our process for clear expectations and standards with respect to other types of recalls, such as those undertaken by McNeil.

We will continue to work with Congress to secure additional authorities that could assist us in assuring product quality and acting more quickly when product quality issues occur. FDA will also be considering enforcement actions in this case as part of the Agency's ongoing changes in enforcement. FDA Commissioner Dr. Margaret Hamburg has called for FDA's enforcement to be "vigilant, strategic, quick, and visible." A range of activities are underway at the Agency to bring this vision to reality, including strengthening our criminal enforcement of FDA's laws.

As we continue these efforts, as well as our other regulatory work, we will focus on entire companies and their systems in addition to focusing on specific violations, individuals, and sites, much as we are doing in the McNeil situation.

Conclusion

Thank you for the opportunity to explain FDA's oversight of drug manufacturing and our engagement with McNeil. I look forward to your questions.