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Anti-Counterfeit Drug Initiative

Merck & Co., Inc is a leading worldwide, human health products company. Through a combination of the best science and state-of-the-art medicine, Merck's Research and Development (R&D) pipeline has produced many important pharmaceutical products available today. These products have saved the lives of or improved the quality of life for millions of people globally.

The well-founded confidence that patients have in the medicines they take must be protected. Regrettably, we have witnessed recently a sharpening of criminal focus on the world's supply of medicines as a target for counterfeiting activity. Highly sophisticated counterfeiters are contaminating the pharmaceutical distribution chain with fakes containing no active ingredients, diluted active ingredients, outdated components and/or contaminated replacements disguised to resemble the true, legitimate product.

FDA has taken an aggressive stand in the battle against the growing threat of counterfeit drugs. The establishment of the FDA Counterfeit Drug Task Force in July 2003 together with the release of its interim report in October 2003 and the sponsoring of a public forum on October 15, 2003 to discuss issues and technologies relating to its anti counterfeiting strategy, reflect FDA's rapid response to a critical safety issue for the American people, and appropriate engagement to fight the crime of counterfeiting medicines.

GENERAL COMMENTS

Merck & Co., Inc. strongly supports the establishment of FDA's Counterfeit Drug Task Force and applauds the Agency for its efforts against this crime whose principal victims are the sick and vulnerable. Merck supports FDA initiatives to identify, deter and halt criminal activity in the counterfeiting of medicines. We fully agree that there is no single deterrent that will eliminate counterfeiting and that a multi-pronged approach, with technology solutions determined by the manufacturer for each of its products, will be the optimal strategy. All methods should be reviewed periodically and revised as necessary to maintain effectiveness.

Many pharmaceutical companies have already implemented anti-counterfeiting technologies into their manufacturing and packaging processes. These technologies may only be known to a few individuals within the company and possibly the FDA (and local authorities in other countries). We must continue to allow the choice of technology to reside with the manufacturer, who is best equipped to determine what is most appropriate to protect the integrity and reputation of each of its products.

It is also important to implement broader strategies and tools that will complement those of the manufacturer, looking both at the shorter and longer term. Many technologies that are currently being reviewed and assessed will be longer term solutions to the problem of counterfeiting. However, to protect the supply of lifesaving medicines now, some immediate actions should also be taken. These would include increased monitoring of the products flowing through our borders, much tougher criminal penalties for counterfeiters, the effective implementation of paper pedigrees nationwide, increased Federal oversight of wholesale, distributor and repackaging operations, and consumer education and notification. We describe each of these options in further detail below.

In addition, as Commissioner McClellan explained in a recent speech at the National Press Club on October 20, 2003, the opening of U.S. borders to the import of foreign medicines will simultaneously open up new paths for unsafe medicines to infiltrate the U.S. drug supply and will make the task of protecting our nation's products from counterfeiting even more difficult. As has been documented in the FDA's Counterfeit Drug Task Force Interim Report (October 2003), counterfeit medicines have already infiltrated many a foreign nation's drug supply. We applaud FDA for continuing to oppose efforts to weaken our nation's border controls and believe it is critical that FDA retain its authority to control the entry of pharmaceutical products into the US and to receive the resources it needs to enforce the existing law.

IMMEDIATE ACTIONS REQUIRED TO HELP PROTECT THE PHARMACEUTICAL SUPPLY CHAIN

Increased FDA Resources to Enforce Laws Against Counterfeit Medicines, Sourced from Within the US or Abroad

As an immediate first step, Merck believes Congress should provide FDA with the resources and authority it needs to ensure our drug supply is secure. As FDA has documented, our nation's drug supply is becoming increasingly threatened by sophisticated counterfeiters. Merck believes FDA should be given the resources it needs to adequately police potential entry points for counterfeit products and to inspect, test and block the distribution of drugs it thinks are unsafe.

Increased Criminal Penalties

In parallel, Merck supports passage of legislation that would strengthen criminal penalties for those convicted of counterfeiting pharmaceutical products, with the sentences being commensurate with the harm (or potential harm) caused to patients. Tough criminal penalties also are deterrents to crime; the current maximum penalty specified in the FD&C Act for counterfeiting pharmaceuticals is only 3 years, far less than criminal penalties for distribution of harmful, illegal drugs such as cocaine. Convictions for counterfeiting medicines should be well publicized to serve as warnings to criminals of the tough approach toward this crime. Members of our industry and our trade associations would be eager to support FDA in its efforts to seek new legislation in this area.

Implementation of the Paper Pedigree

Merck supports the implementation of the 21 CFR 203.50 requirement for paper pedigrees for pharmaceutical products along with verification of the documents by the purchaser. This regulation has never been officially implemented even though authorized by the Prescription Drug Marketing Act of 1987. These "passports" for medicines are designed to provide a paper trail verifying the distribution chain for each lot of product. While the papers themselves may be counterfeited, the requirement for

paper pedigrees is an additional barrier to fake medicines entering the distribution system. A critical element of the success of the paper pedigree is ownership of the verification. Verification of the paper pedigree cannot be a simple "rubber stamp" at each stop of the product along the distribution chain. Critical reviews of the document at each distribution point, along with signatures of receipt, are essential steps in support of the effectiveness of the pedigree approach. In the future, if pedigree papers become electronic, effective processes put in place for the paper version will be essential for the success of an electronic system. Ultimately we would be in favor of an electronic pedigree to replace the paper system but neither the technology nor the infrastructure is currently available to implement an electronic system.

Increased Federal Oversight of Wholesaler, Distributor and Repackager

In recent criminal investigations of counterfeiting activity, repackagers were noted to be the weakest link in the distribution system. Repackaging involves the removal of product from the original container filled by the manufacturer. The product is then repacked into a new container chosen by the repackager and marketed for further distribution. This practice eliminates any anti-counterfeiting technology integral to the original packaging. At present, major repackaging companies may contract with firms such as Merck to include anti-counterfeiting technology (or other technologies) in the repackaged product but, this is not the case with all repackagers.

Merck requests that FDA consider tighter controls on repackagers, such as increased federal scrutiny of their internal processes, cGMPs, product accountability, sourcing practices (secure business practices) and similar requirements for anti-counterfeiting deterrents that manufacturers may be required to meet. Major repackaging companies are already subject to the same FDA manufacturing and packaging oversight as pharmaceutical manufacturers. Merck has visited such repackaging companies and found them to meet Merck's high standards for product control. We request that all repackagers be subject to the same high standards of law. We also believe that the FDA needs to work with the states to tighten license controls and requirements for wholesalers and distributors, and specifically secondary distributors.

Education and Notification

Consumers need to be educated about the problem of counterfeit medicines and what to do if they find their medicine looks, tastes or feels different (in both the product or the package) or if the product does not appear to have the intended effect.

FDA has suggested that suspect counterfeit medicines might be reported via the MedWatch system. Merck believes that this mechanism for reporting would be cumbersome for the consumer and would dilute the primary purpose of the system (to report adverse events, medical errors or complaints). The current system of reporting counterfeits does need improvement, however; the public needs to be informed of what to do if they encounter suspect medicines. We urge the FDA and Department of Justice to immediately notify the pharmaceutical company affected of any investigation initiated on one of their products.

Members of PhRMA (The Pharmaceutical Research and Manufacturers of America) including Merck & Co., Inc., have already committed on a voluntary basis to notify FDA within 5 working days of determining that there is a reasonable belief that a product has been counterfeited. To augment this process, we support the establishment of a counterfeiting 'hotline' into the FDA, whose existence would be widely publicized and made easily accessible to patients, physicians, distributors, pharmacies and the pharmaceutical industry. Reports of counterfeit medicines into this hotline should be triaged and evaluated by FDA, and the pharmaceutical manufacturer informed as soon as possible if an investigation will be initiated.

TECHNOLOGY-BASED DETERRENTS

Technology solutions to deter counterfeiting are in development and include both packaging aspects and deterrents integral to the products themselves. Merck believes that the choice of anti-counterfeit technology should be left to the manufacturer who is the expert in the development, manufacture and design of both the product and the packaging components. Additionally, if the implementation of the technology (such as adding deterrents integral to the product) requires regulatory approval, Merck requests that FDA consider reducing regulatory reporting categories and regulatory requirements, such as minimization of stability requirements, as appropriate, so that timely changes can be made to safeguard the supply chain. There should be a phase-in period for any regulation that is instituted, with prioritization of initial products determined jointly by both FDA and industry. Ultimately, all pharmaceutical products should be subjected to the same set of anti-counterfeiting standards. In this way, the integrity of the whole supply chain (and the public's confidence in it) can be maintained.

Unit of Use Packaging

Merck strongly believes that unit of use packaging such as blister packs is not the solution to deter counterfeiting activity. Counterfeit medicines enclosed in blister packaging made to resemble the original manufacturer's packaging have been identified during recent international counterfeiting investigations. The sophistication of the criminal element cannot be underestimated, if it can be seen, it can be counterfeited. Requirements for unit of use packaging will not solve the problem. In fact, with certain complicated dosing regimens, the unit of use package may contain multiple tablets, of different strengths, required for the specific patient dose. It would be impossible for a manufacturer to personalize each unit of use package, required for the patient's individualized dose, in a timely manner.

Track and Trace System

An electronic 'Track and Trace' system has been touted as the answer to the problem of counterfeit products entering the distribution chain. Merck agrees that a truly closed system would probably be a powerful deterrent to bogus medicines entering the distribution system and could help to identify suspicious activity. Effective technology is many years away from implementation, however. For example, scanners would need to be installed at every step of the distribution chain, but only a small percentage of the supply chain uses scanners at present.

In addition, an information technology infrastructure must be established to verify and validate the serialized numbers placed on each unit package. The scope of this system would be far greater than any currently in operation, such as FEDEX, and any system would need to be fully tested and validated. It has been estimated that one major US pharmaceutical company puts one billion unit packages into distribution annually. With Track and Trace, each of the one billion packages would need to be tagged and the data emitted from the tag validated at each distribution stop.

Finally, the information "tags" on each unit of distribution would need to be read without error by the scanners. Current system designs, however, have demonstrated difficulties in transmitting and receiving data from the information tags in certain standard configuration of bottle packs or if the product is in a liquid form (liquid may block the transmission from the "tag"). The rate of errors for existing technology is currently too high for any available system to be seriously considered as a viable option.

Current technologies need to be refined before an infrastructure can effectively be implemented. In addition, the business model needs further development (for example, should a third party broker be responsible, should there be a National system?) and needs evaluation especially with respect to cost-sharing by all parties involved in the distribution of product. We propose that the evaluation of the

business model begin immediately as part of the FDA Task Force remit, and include expert input from representatives of all elements of the supply chain.

CONCLUSION

In summary, Merck & Co., Inc. strongly supports FDA's efforts against the counterfeiting of medicines. We are committed to working with the agency in finding solutions, both immediate and longer-term, to diminish the threat of this crime.

The crime of counterfeiting has at least three victims: the first and most important is the patient who is denied the benefit of the medicine and may be harmed or killed by this crime; the healthcare system suffers too, through an erosion of public confidence and also an increase in costs as it devotes scarce resources to treating people harmed by counterfeits; and finally the pharmaceutical manufacturer is also harmed, as its reputation may be unfairly affected.

We agree that there is no single "magic bullet" to prevent counterfeiting of pharmaceuticals and that a multi-pronged approach is required to address this serious problem. No approach will be foolproof, however. Even with a multi-pronged approach continued vigilance is necessary. As we have stated above, all methods should be reviewed periodically and revised as necessary to maintain effectiveness. The pharmaceutical manufacturer is the most knowledgeable about the development, processing, packaging and distribution of each product and is therefore the best suited to determine the best anti-counterfeiting tool and strategies to employ.

A truly closed distribution system, as outlined by the Track and Trace initiative, has potential to be a powerful tool to halt and prevent counterfeiting. The Track and Trace system, however, requires further development of technology and business ideas which may take years. Moreover, any system is only as good as its components, "tags", scanners, databases and their users must also be under control to prevent counterfeiting.

To protect immediately the integrity of the pharmaceutical supply chain, we suggest the following steps be taken:

- Increase resources to FDA to continue to enforce laws against counterfeit medicines sourced from within the US or abroad,
- Tougher criminal penalties for those convicted of counterfeiting pharmaceuticals,
- Implementation of the paper pedigree system with verification,
- Expansion of Federal oversight to include wholesale, distribution and all repackaging operations, which should be subject by law to the same high standards as manufacturers,
- Education of consumers and patients on what to do if counterfeiting is suspected including the establishment of a national hot line.

We appreciate the opportunity to share our comments with respect to FDA's Counterfeit Drug Task Force Interim Report. Please do not hesitate to contact me should you have any questions.

Sincerely,

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