COMBATING COUNTERFEIT DRUGS

A REPORT OF THE FOOD AND DRUG ADMINISTRATION

February 18, 2004

SAFE AND SECURE

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EXECUTIVE SUMMARY

The counterfeiting of currency and consumer products are common problems that plague governments and manufacturers around the world, but the counterfeiting of medications is a particularly insidious practice. Drug counterfeiters not only defraud consumers, they also deny ill patients the therapies that can alleviate suffering and save lives. In some countries the counterfeiting of drugs is endemic—with some patients having a better chance of getting a fake medicine than a real one. In many more countries, counterfeit drugs are common. In the United States, a relatively comprehensive system of laws, regulations, and enforcement by Federal and state authorities has kept drug counterfeiting rare, so that Americans can have a high degree of confidence in the drugs they obtain through legal channels. In recent years, however, the FDA has seen growing evidence of efforts by increasingly well-organized counterfeiters backed by increasingly sophisticated technologies and criminal operations to profit from drug counterfeiting at the expense of American patients.

To respond to this emerging threat, Commissioner of Food and Drugs Mark McClellan formed a Counterfeit Drug Task Force in July 2003. That group received extensive comment from security experts, Federal and state law enforcement officials, technology developers, manufacturers, wholesalers, retailers, consumer groups, and the general public on a very broad range of ideas for deterring counterfeiters. Those comments reinforced the need for FDA and others to take action in multiple areas to create a comprehensive system of modern protections against counterfeit drugs. FDA discussed those ideas, and considered alternatives and criticisms at its public meetings, to develop a comprehensive framework for a pharmaceutical supply chain that will be secure against modern counterfeit threats. The specific approach to assuring that Americans are protected from counterfeit drugs includes the following critical elements:

1) Implementation of new technologies to better protect our drug supply.

Because the capabilities of counterfeiters continue to evolve rapidly, there is no single “magic bullet” technology that provides any long-term assurance of drug security. However, a combination of rapidly improving “track and trace” technologies and product authentication technologies should provide a much greater level of security for drug products in the years ahead. Similar anti-counterfeiting technologies are being used in other industries, and FDA intends to facilitate their rapid development and use to keep drugs secure against counterfeits.

a. The adoption and common use of reliable track and trace technology is feasible by 2007, and would help secure the integrity of the drug supply chain by providing an accurate drug "pedigree," which is a secure record documenting the drug was manufactured and distributed under safe and secure conditions.

Modern electronic technology is rapidly approaching the state at which it can reliably and affordably provide much greater assurances that a drug product was manufactured safely and distributed under conditions that did not compromise its potency. FDA has concluded that this approach is a much more reliable direction for assuring the legitimacy of a drug than paper recordkeeping requirements, which are more likely to be incomplete or falsified, and that it is feasible for use by 2007. Radiofrequency Identification (RFID) tagging of products by manufacturers, wholesalers, and retailers appears to be the most promising approach to reliable product tracking and tracing. Significant feasibility studies and technology improvements are underway to confirm that RFID will provide cost-reducing benefits in areas such as inventory control, while also providing the ability to track and trace the movement of every package of drugs from production to dispensing. Most importantly, reliable RFID technology will make the copying of medications either extremely difficult or unprofitable. FDA is working with RFID product developers, sponsors, and participants of RFID feasibility studies to ensure that FDA's regulations facilitate the development and safe and secure use of this technology. FDA is also working with other governmental agencies to coordinate activities in this area.

b. Authentication technologies for pharmaceuticals have been sufficiently perfected that they can now serve as a critical component of any strategy to protect products against counterfeiting.

Authentication technologies include measures such as color shifting inks, holograms, fingerprints, taggants, or chemical markers embedded in a drug or its label. The use of one or more of these measures on drugs, starting with those considered most likely to be counterfeited, is an important part of an effective anti-counterfeiting strategy. Because counterfeiters will adapt rapidly to any particular measure and because the most effective measures differ by product, the most effective use of authentication technology will vary by drug product over time. FDA intends to clarify its policies and procedures to help manufacturers employ and update these technologies safely and effectively. In particular, FDA plans to publish a draft guidance on notification procedures for making changes to products (e.g., addition of taggants), their packaging, or their labeling, for the purpose of encouraging timely adoption and adaptation of effective technologies for detecting counterfeit drugs. FDA also intends to continue to evaluate and provide information to stakeholders

on forensic technologies (e.g., use of product fingerprinting, addition of markers) and other analytical methods that allow for rapid authentication of drug products. FDA also plans to support the development of criteria that contribute to counterfeiting risk, and/or the development of a national list of drugs most likely to be counterfeited based on these criteria, to assist stakeholders in focusing their use of anti-counterfeiting technologies as effectively as possible.

2) Adoption of electronic track and trace technology to accomplish and surpass the goals of the Prescription Drug Marketing Act

At the time PDMA was enacted the only way to pass on a pedigree for drugs was to use paper, which has posed practical and administrative challenges. RFID technology, which would provide a *de facto* electronic pedigree, could surpass the intent of PDMA and do so at a lower cost. In light of the rapid progress toward much more effective electronic pedigrees that can be implemented within several years, FDA intends to continue to stay its regulations regarding certain existing pedigree requirements to allow suppliers to focus on implementing modern effective pedigrees as quickly as possible.

3) Adoption and enforcement of strong, proven anti-counterfeiting laws and regulations by the states.

Because states license and regulate wholesale drug distributors they have an important role in regulating the drug distribution supply chain. The FDA is working with the National Association of Boards of Pharmacy on its effort to develop and implement revised state model rules for licensure of wholesale drug distributors. Such rules will make it difficult for illegitimate wholesalers to become licensed and transact business, thus making it easier to deter and detect channels for counterfeit drugs. Some states have already reduced counterfeit threats by adopting such measures. FDA will continue working with NABP and states to facilitate adoption of the Model Rules.

4) Increased criminal penalties to deter counterfeiting and more adequately punish those convicted.

Although increased criminal penalties would not affect FDA's regulatory framework for overseeing the U.S. drug supply, they would provide an added deterrent to criminals who work to counterfeit our citizens' medications. FDA has requested that the United States Sentencing Commission amend the sentencing guidelines to increase substantially the criminal penalties for manufacturing and distributing counterfeit drugs and to provide for enhanced penalties based on the level of risk to the public health involved in the offense.

5) Adoption of secure business practices by all participants in the drug supply chain.

Effective protection against counterfeit drugs includes actions by drug producers, distributors, and dispensers to secure their business practices such as ensuring the legitimacy of business partners and refusing to do business with persons of unknown or dubious background, taking steps to ensure physical security, and identifying an individual or team in the organization with primary responsibility for ensuring that effective security practices are implemented. The wholesalers have already drafted a set of secure business practices and FDA will continue to work with other major participants of the drug supply chain to develop, implement, and disseminate such business practices, through such steps as issuing guidance and supporting the development of industry best practices. To help ensure secure business practices, FDA intends to increase its inspection efforts of re-packagers whose operating procedures place them at increased risk for the introduction of counterfeit drugs.

6) **Development of a system that helps ensure effective reporting of counterfeit drugs to the agency and that strengthens FDA's rapid response to such reports.**

If counterfeit drugs do enter the American marketplace, procedures should be in place to recognize the hazard and alert the public quickly and effectively. FDA plans to take new steps to encourage health professionals to report suspected counterfeit drugs to FDA's MedWatch system. FDA also intends to create a Counterfeit Alert Network to provide timely and effective notification to affected health professionals and the public whenever a counterfeit drug is identified.

7) **Education of consumers and health professionals about the risks of counterfeit drugs and how to protect against these risks.**

FDA will develop educational materials, including new tools on the FDA website at www.fda.gov, new public service announcements, and new educational partnerships with consumer and health professional organizations, to help consumers avoid counterfeits. FDA will enhance its educational programs for pharmacists and other health professionals about their role in minimizing exposure to, identifying, and reporting counterfeits.

8) **Collaboration with foreign stakeholders to develop strategies to deter and detect counterfeit drugs globally.**

Counterfeit drugs are a global challenge to all nations, and criminal counterfeiting operations are increasingly operating across national borders. FDA intends to work with the World Health Organization, Interpol, and other international public health and law enforcement organizations to develop and implement worldwide strategies to combat counterfeit drugs.

The steps described in this report are intended to secure the safety and of the U.S. drug supply, which the FDA regulates. The FDA does not have the legal authority or resources to assure the safety and efficacy of drugs purchased from other countries outside our domestic drug distribution system, or from unregulated Internet sites that are not run by pharmacies licensed and regulated by U.S. states.

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A. Purpose of the Anti-Counterfeiting Initiative

The actions described in this report are based on the work of an internal FDA Counterfeit Drug Task Force[1], which was formed in July 2003 by Commissioner of Food and Drugs Mark McClellan, M.D., Ph.D., with the goals of:

- Preventing the introduction of counterfeit drugs and biologics into the U.S. drug distribution chain;
- Facilitating the identification of counterfeit drugs and biologics;
- Minimizing the risk and exposure of consumers to counterfeit drugs and biologics; and
- Avoiding the addition of unnecessary costs to the prescription drug distribution system, or unnecessary restrictions on lower-cost sources of drugs.

B. Scope of the Problem

FDA believes that counterfeiting is not widespread within the system of manufacturing and distributing pharmaceuticals legally in the United States, as a result of an extensive system of federal and state regulatory oversight and steps to prevent counterfeiting undertaken by drug manufacturers, distributors, and pharmacies. However, the agency has recently seen an increase in counterfeiting activities as well as increased sophistication in the methods used to introduce finished dosage form counterfeits into the otherwise legitimate U.S. drug distribution system. FDA counterfeit drug investigations have increased to over 20 per year since 2000, after averaging only 5 per year through the late 1990's. (See Figure 1 -- Chart of FDA investigations) Increasingly, these investigations have involved well-organized criminal operations that seek to introduce finished drug products that may closely resemble legitimate drugs yet may contain only inactive ingredients, incorrect ingredients, improper dosages, sub-potent or super-potent ingredients, or be contaminated. Thus, drug counterfeiting poses real public health and safety concerns today, and may pose an even greater threat in the future if we fail to take preventative measures now. As counterfeiters continue to seek out new technologies to make deceptive

[1] The Task Force consists of senior agency staff from the Office of the Commissioner (Office of Policy and Planning, Office of External Affairs, and Office of the Chief Counsel), Office of Regulatory Affairs, the Center for Drug Evaluation and Research, and the Center for Biologics Evaluation and Research.

products and introduce them into legitimate commerce, our systems for protecting patients must respond effectively.

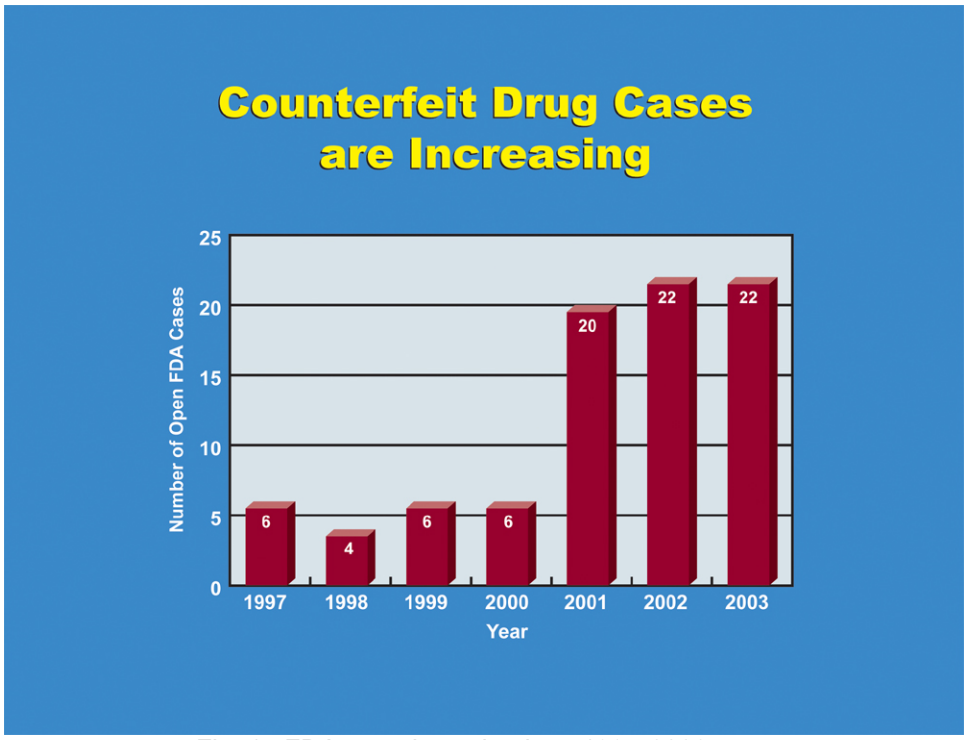


Fig. 1: FDA open investigations 1997-2003

Although exact prevalence rates in the U.S. are not known, outside the U.S. drug counterfeiting is known to be widespread and affect both developing and developed countries. In some countries more than half of the drug supply may consist of counterfeit drugs. For example, recent reports have detailed that more than 50% of anti-malarials in Africa are believed to be counterfeit. In virtually all countries, counterfeit drug operations have been uncovered in recent years.

C. What is in this Report

The body of this report contains a range of findings that have broad support from industry stakeholders and the public to identify and address the vulnerabilities in the U. S. drug distribution system to counterfeit drugs.

This report is based on the potential options discussed in the Task Force's Interim Report, the comments FDA received in response to that report, our internal discussions, and on information gathered and reviewed by the Task Force including:

- Meetings with government agencies, manufacturers, wholesalers, retailers, professional and trade associations, standard-setting

organizations, consumer groups, and manufacturers of anti-counterfeiting measures;
- Reviewing reports prepared by, or on behalf of, federal and state governments;
- Sponsoring a public meeting where 72 presentations were made
- Sponsoring a technology forum which included 54 exhibits
- Reviewing public comments to the anti-counterfeiting initiative docket
- Site visits to manufacturing facilities, wholesale distribution centers, retailers, radio-frequency identification (RFID) laboratories and pilot facilities;
- Attendance at stakeholder task force meetings and industry RFID feasibility study meetings
- Meetings with academic and industry experts

Appendix A contains the Counterfeit Alert Network Co-sponsorship agreement. See www.fda.gov/oc/initiatives/counterfeit/ for background information that was included in the Task Force's Interim Report (released on October 2, 2003) as well as a detailed discussion of the comments FDA received. Appendix B contains a more detailed discussion of the comments FDA received and considered in developing the final report.

The FDA is grateful for the input and universal support, not only with regard to the creation of the task force, but also with regard to the need for securing the nation's drug supply.

D. Securing our Nation's Drug Supply

To secure the U. S. drug supply chain, there are several areas that deserve attention, including the areas of technology, business practices, legislation, regulation, public awareness and education, creation of an alert network, and international cooperation.

1. TECHNOLOGY

a. Unit of Use Packaging

1) What FDA sought comment on:

- Whether to package all finished dosage form drugs in unit of use packaging as appropriate for the particular product (e.g., tablet, multi-dose vial) at the point of manufacture?

2) What the comments said:

Comments cited a large number of benefits, including eliminating the need for re-packaging and improved patient compliance, as well as a large number of costs,

including those associated with shifting production from bulk packaging. The cost hurdle to counterfeiters, created by unit of use packaging, was said not to be high enough for it to be effective as a stand-alone anti-counterfeiting measure. A detailed discussion of the comments is in Appendix B.

3) Discussion:

Although single unit containers (e.g., blister packs) usually come to mind, unit of use packaging is any container closure system designed to hold a specific quantity of drug product for a specific use and dispensed to a patient without any modification except for the addition of appropriate labeling.

Unit of use packaging does not create a sufficiently high level of security to justify its use as a stand-alone anti-counterfeiting measure. However, because of its many other benefits, which may vary on a product specific basis (e.g., tablets, liquid forms), manufacturer initiated cost-benefit analyses of particular products, starting with newly approved products and products that are likely to be counterfeited, are likely to show that unit of use packaging could be effective as one layer in a multi-layered anti-counterfeiting strategy.

4) FDA Conclusions:

Unit of use packaging can be beneficial in fighting counterfeit drugs.

- It would be beneficial for all manufacturers and re-packagers to analyze the costs and benefits of using unit of use packaging for each product, starting with newly approved products and products that are likely to be counterfeited, and to consider implementing unit of use packaging for products where the benefits are equal to or outweigh the costs;
- Unit of use packaging can be helpful, but only as one layer in a multi-layered anti-counterfeiting strategy;
- FDA intends to encourage adoption of unit of use packaging by: inviting stakeholders and other interested individuals and organizations to submit research on the relative costs and benefits of unit of use packaging to assist FDA in developing future policy; and encouraging standard setting bodies to develop standards for unit of use packaging with the goal of reducing its costs (e.g., in areas such as size, shape, and pill organization).

b. Tamper Evident Packaging

1) What FDA sought comment on:

- Whether to use tamper evident packaging from the point of manufacture, for all dosage forms, active pharmaceutical ingredients (APIs), and bulk chemicals?

2) What the comments said:

The comments on tamper evident packaging mirrored the comments on unit of use packaging.

3) Discussion

Decisions to employ tamper evident packaging on prescription drug containers as an anti-counterfeiting measure require a product specific cost-benefit analysis. As with unit of use packaging, FDA does not believe that tamper evident packaging presents a high enough hurdle for counterfeiters to make it effective as a stand-alone anti-counterfeiting measure.

4) FDA Conclusions:

Tamper evident packaging may be beneficial in fighting counterfeiting of prescription drugs.

- It would be beneficial for manufacturers and re-packagers to consider using tamper evident packaging for prescription product containers, starting with products likely to be counterfeited or newly approved products, where the benefits are equal to or outweigh the costs;
- Tamper evident packing can be helpful, but only as one layer in a multi-layered anti-counterfeiting strategy.

c. Authentication Technology

1) What FDA sought comment on:

- Whether to incorporate at least two types of anti-counterfeiting technologies into the packaging and labeling of all drugs, at the point of manufacture, with at least one of those technologies being covert (i.e., not made public, and requiring special equipment or knowledge for detection) starting with those products at high risk of being counterfeited and where the introduction of counterfeit product poses a serious health risk;
- Whether to incorporate a taggant, chemical marker, or other unique characteristic(s) into the manufacturing process of all drugs that is only identifiable with the use of sophisticated analytic techniques starting with those products at high risk of being counterfeited and where the introduction of counterfeit product poses a serious health risk; and

- Whether to issue FDA guidances concerning the appropriate use of anti-counterfeiting technologies and the application and review process for labeling and packaging changes or product changes such as incorporation of taggants, chemical markers, or other unique characteristic(s) into the product for the purpose of product authentication.

2) What the comments said:

The comments stressed that there was no "silver bullet" anti-counterfeiting technology because sophisticated, well-financed counterfeiters can defeat any anti-counterfeiting measure. Therefore, the best strategy is to use multiple, periodically changing, authentication measures on a product specific basis after doing a risk analysis that takes into account the risk that the product will be counterfeited and the public health risk if the product is counterfeited.

Given the rapid developments in anti-counterfeiting technology and the dangers of aiding counterfeiters by locking in or requiring certain technologies, most comments stressed that the FDA should not mandate the use of specific anti-counterfeiting technologies.

FDA issuance of guidance concerning the agency's application and notification policies and procedures related to incorporating anti-counterfeiting measures into products (e.g., taggants) or labeling and packaging (e.g., inks, holograms) was universally supported.

A detailed discussion of the comments is in Appendix B.

3) Discussion:

FDA agrees that the danger of unwittingly assisting counterfeiters and stifling technologic development outweigh the benefits that would accrue if it were to mandate the use of a specific authentication technology at this time. Furthermore, the decision to deploy authentication technologies is best made by the manufacturer, based on a product specific risk-benefit analysis that, in the future, should take into account whether mass serialization and radio-frequency identification technology (see below) is being used for tracking and tracing the drug.

However, due to the high costs and technical barriers that authentication technologies create for counterfeiters, their use is a critical component of any effective multi-layered anti-counterfeiting strategy, especially for products that are likely to be counterfeited. Therefore, FDA believes that an appropriate role for it is to facilitate the use of authentication technologies by reducing any regulatory hurdles that may exist relating to their use.

4) FDA Conclusions:

Existing authentication technologies have been sufficiently perfected they can now serve as a critical component of any strategy to protect products against counterfeiting.

- The use by manufacturers and re-packagers of one or more authentication technologies on their products, particularly those likely to be counterfeited, would protect the public health and diminish counterfeiting;
- To facilitate the use of authentication technologies on existing products, FDA plans to publish a draft guidance on notification procedures for making changes to products (e.g., addition of taggants), their packaging, or their labeling for the purpose of deterring and detecting counterfeit drugs;
- FDA plans to continue to evaluate and disseminate information to stakeholders on developing forensic technologies (e.g., use of product fingerprinting, addition of markers) and other analytical methods that allow for rapid authentication of drug products.

d. Identification of Products likely to be counterfeited

1) What FDA sought comment on:

- Are all products at high risk for being counterfeited?
- How can products at high risk for being counterfeited be identified?
- What criteria should be used to determine if a product is at high risk for being counterfeited?

2) What the comments said:

Although a few comments suggested that all products were at high risk for being counterfeited, most of the comments FDA received supported the idea of developing criteria by which stakeholders could determine which products are likely to be counterfeited and/or developing a national list of products likely to be counterfeited based on these criteria. There was general agreement that the existence of state specific lists, each with its own regulatory requirements, could inhibit commerce and adversely affect the availability of drugs. FDA notes that the State of Florida has already published a list of “specified products” (i.e., a list of drugs most likely to be counterfeited) that is being used to implement state pedigree requirements. A detailed discussion of the comments is in Appendix B.

3) Discussion:

Due to the large number of drugs with the potential to be counterfeited, FDA does not believe it is possible to create a comprehensive list of all such drugs. However, FDA does believe that a national list of those drugs most likely to be counterfeited and/or a set of criteria to use for determining those drugs would be useful for stakeholders to use at their discretion. Uses could include:

- Assisting manufacturers and re-packagers in making decisions whether to use authentication technologies and unit of use packaging;
- Assisting wholesalers in developing purchasing policies and allocating resources for detecting counterfeits;
- Assisting retailers in targeting certain drugs for authentication and patient education prior to dispensing;
- Assisting states in implementing regulatory requirements;
- Assisting stakeholders in developing migratory paths to adoption of mass serialization and electronic track and trace technology.

FDA strongly supports the development of such a set of criteria, or a list based on these criteria, that has the support and participation of all stakeholders. Regular input from interested parties as well as the ability to add or delete drugs from the list on short notice are important parts of the process.

FDA believes that members of regulated industry are better positioned at this time than FDA to develop a process for creating, maintaining, and updating such a list (and/or set of criteria).

4) FDA Conclusions:

FDA has concluded that there would be great value in the creation of a national list of drugs most likely to be counterfeited based on factors that are likely to contribute to counterfeiting risk.

- FDA intends to encourage stakeholders and standards setting organizations to work together to create a national list of drugs most likely to be counterfeited, based on an assessment of criteria for determining counterfeit risk;
- The best result would be achieved if all stakeholders, including FDA, and other interested parties participate in developing a list, or criteria for determining, drugs most likely to be counterfeited;
- Any such list, and/or criteria, would be most effective if made publicly available to all stakeholders.

FDA is aware of only one national list of drugs most likely to be counterfeited. The list was developed by the National Association of Boards of Pharmacy and is available at www.nabp.org.

e. Radio-frequency Identification (RFID) Technology

1) What FDA sought comment on:

- Whether a pedigree for all drug products can be achieved by phasing in track and trace technology (i.e., electronic pedigree) starting at a case and pallet level for products likely to be counterfeited and progressively including all products at the case, pallet, and package level; and
- Whether, as an interim measure, prior to widespread adoption of track and trace technology all drugs and biologics likely to be counterfeited should be tracked and traced either by limiting the number of transactions of the product or by using available track and trace technology, identifying the drug at the case and pallet level, and preferably at the product level, throughout the distribution system.

2) What the comments said:

There was universal support for the adoption of electronic track and trace technology. RFID was cited as being the technology with the strongest potential for securing the supply chain but that it was not ready for widespread commercial use with pharmaceutical products. Many costs, potential benefits, and unresolved issues related to RFID were cited. The potential benefits included the ability to control inventory and conduct rapid, efficient recalls, while costs that could hinder the adoption of RFID included purchase of tags and other hardware, integration into existing information systems, and compliance with regulatory requirements (e.g., labeling, electronic records). Important unresolved issues included the need to develop standards and business rules for RFID, the need to address database management issues, and the need to determine the effect of RFID on product quality.

FDA was also informed that some companies are planning feasibility studies concerning business uses of RFID for early this year and that other activities related to creating standards, business rules, and migratory pathways for RFID are also ongoing. A detailed discussion of these activities and other comments concerning RFID is in Appendix B.

3) Discussion

Use of mass serialization to uniquely identify all drug products intended for use in the United States is the single most powerful tool available to secure the U. S. drug supply. Mass serialization involves assigning a unique number (the

electronic product code or EPC) to each pallet, case, and package of drugs and then using that number to record information about all transactions involving the product, thus providing an electronic pedigree from the point of manufacture to the point of dispensing. This unique number would allow each drug purchaser to immediately determine a drug's authenticity, where it was intended for sale, and whether it was previously dispensed.

Although there is general agreement that widespread use of mass serialization is inevitable, several important issues remain unresolved, including the migratory path(s) that participants in the drug distribution system will follow as they begin to serialize their products, and the most likely timeline for widespread commercial use.

It currently appears that the technology most likely to bring mass serialization into widespread commercial use by the pharmaceutical industry is RFID, although two-dimensional bar codes may be used for some products. RFID technology includes not only the silicon tags containing the EPC, but also antennas, tag readers, and information systems that allow all users to identify each package of drugs and its associated data. This data can be used not only to authenticate drugs but also to manage inventory, conduct rapid, targeted recalls, prevent diversion, and ensure correct dispensing of prescriptions.

Acquiring and integrating RFID technology into current manufacturing, distribution, and retailing processes will require considerable planning, experience, and investment of resources. Currently, some manufacturers, wholesalers, and retailers are developing business plans and testing mass serialization using RFID while others are taking a wait and see approach. Due to rapid technologic advancements, the lack of significant market place experience with it in the pharmaceutical supply chain, each participant is best situated to determine his optimal path(s) to adopting it.

Therefore, FDA has identified near term actions, described below, for it to take in order to facilitate the performance of mass serialization feasibility studies using RFID, and to assist stakeholders as they migrate towards the use of RFID technology.

In the long term, after there is significant market place experience with RFID, FDA plans to propose or clarify, as necessary and appropriate, policies and regulatory requirements relating to the use of RFID. Labeling, electronic records, product quality, and Current Good Manufacturing Practices (cGMP) requirements are issues that have arisen in connection with RFID. However, regulatory or policy determinations regarding these, or other, issues should not be made until they can be informed by sufficient data and significant marketplace experience with RFID. FDA has also identified a series of actions, discussed below, that would help industry stakeholders and standard-setting organizations achieve this goal.

Lastly, stakeholders will need to ensure that they comply with the patient privacy protections provided by the Health Insurance Portability and Accountability Act as they implement use of RFID technology.

4) FDA Conclusions:

The adoption and common use of RFID as the standard track and trace technology, which is feasible in 2007, would provide better protection.

- Due to industry's current initiatives, mass serialization and RFID technology is likely to be adopted according to the following timeline:

January – December 2004

- Performance of mass serialization feasibility studies using RFID on pallets, cases, and packages of pharmaceuticals;

January – December 2005

- Mass serialization of some pallets and cases of pharmaceuticals likely to be counterfeited;
- Mass serialization of some packages of pharmaceuticals likely to be counterfeited; and
- Acquisition and use of RFID technology (i.e., ability to read and use the information contained in RFID tags and the associated database) by some manufacturers, large wholesalers, some large chain drug stores, and some hospitals.

January - December 2006

- Mass serialization of most pallets and cases of pharmaceuticals likely to be counterfeited and some pallets and cases of other pharmaceuticals;
- Mass serialization of most packages of pharmaceuticals likely to be counterfeited; and
- Acquisition and use of RFID technology (i.e., ability to read and use the information contained in RFID tags and the associated database) by most manufacturers, most wholesalers, most chain drug stores, most hospitals, and some small retailers.

January – December 2007

- Mass serialization of all pallets and cases of pharmaceuticals;
- Mass serialization of most packages of pharmaceuticals; and

- Acquisition and use of RFID technology (i.e., ability to read and use the information contained in RFID tags and the associated database) by all manufacturers, all wholesalers, all chain drug stores, all hospitals, and most small retailers.

- FDA plans to assist, to the extent necessary and appropriate, in facilitating the rapid, widespread adoption of RFID in the drug distribution system by working with stakeholders in the following areas:
  --Addressing any regulatory and policy issues related to the performance of feasibility studies;
  --Addressing any regulatory and policy issues relating to the notification requirements associated with implementation of RFID;
  --Addressing any product quality concerns and data issues related to the performance of feasibility studies;
  --Reviewing protocols for feasibility studies;
  --Working with other governmental agencies to coordinate activities;
  --Encouraging stakeholders to convene meetings of supply chain participants to identify, discuss, and propose solutions to technical, business, and policy issues related to the use of RFID technology in the pharmaceutical distribution system; and
  --Exploring the need for any other processes and venues that might be needed to assist stakeholders as they migrate towards the use of RFID technology.
- FDA intends to regularly review the pace at which RFID is being adopted in the U. S. drug distribution system;
- FDA plans to publish or clarify, as appropriate, regulatory requirements, policy guidance, and product quality testing requirements related to the use of RFID after sufficient data and marketplace experience with RFID are available to adequately inform our decision-making; and
- FDA intends to consider taking further steps to facilitate the adoption of mass serialization.

1. Business steps for industry

Each industry stakeholder interested in implementing RFID would benefit from the following steps:

- Create an internal team focused on the adoption of mass serialization and use of RFID technology;
- Perform internal feasibility studies to gain experience with mass serialization and RFID technology and to identify internal business issues requiring resolution;
- Perform external pilot studies with stakeholders across the supply chain to gain experience using mass serialization and RFID and to identify opportunities, barriers and external business issues associated with them;

- Develop policy and a business case for the use of mass serialization and RFID;
- Cooperate and work with other stakeholders and government agencies to develop infrastructure and information systems to use with mass serialization of pallets, cases, and packages of drugs;
- Participate on standard setting groups developing technical standards and business rules for use of mass serialization and RFID;
- Work with government agencies and other members of the supply chain to identify and address regulatory and economic issues that could delay the adoption of mass serialization and RFID; and
- Educate other members of the supply chain and government agencies about mass serialization and RFID.

To the extent possible, it would be most useful for interested firms to perform these actions concurrently. For example, standards development requires knowledge gained from feasibility studies in order to move forward, and vice versa.

2. Standards Setting Issues

Any effort to develop standards for mass serialization of pallets, cases, and packages would be most effective if it addressed the following issues:

- Minimum Information Requirements for the serial number – in the case of RFID tags this means containing a mass serialization code that uniquely identifies the object to which it is attached (e. g., minimum of 96 bits of information);
- Communication protocol standards – in the case of RFID this means standard protocols for interrogating and reading tags;
- Reader Requirements – Readers of mass serialization codes should be interoperable (e. g., readers must use protocols that allow them to read multiple classes of tags or bar codes, as applicable) and should be able to automatically upgrade software over an information network;
- Pedigree requirements – this means that databases containing transaction information should be compatible (e.g., format, mark-up language);
- Information Network Requirements
    1. Database Structure (e .g., centralized vs. distributive)
    2. Data ownership
    3. Data access (to meet business, track and trace, and recall needs)
    4. Data Access controls to assure information security;
- Software Requirements – all applications should be compatible and compliant to assure global interoperability; and
- Best use of Frequencies – (e. g., 13.56 megahertz on packages and 915 megahertz on cases and pallets due to interference and read range issues).

2. REGULATORY INITIATIVES AND STATE MODEL RULES

All levels of government, in addition to the private sector, should take responsibility for ensuring the safety and security of the U.S. drug distribution system. Each level has a role in deterring and preventing the introduction of counterfeit drugs into the nation's drug supply chain. To complement and build on the technology measures described above, regulatory and legislative steps at all levels of government may be necessary. At the Federal level, FDA is taking steps to meet the objectives of the Prescription Drug Marketing Act (PDMA), which is intended to address vulnerabilities in the U.S. drug distribution system. At the State level, it would be beneficial for states to strengthen their provisions governing wholesale distribution, as described below in the revised Model Rules for Licensure of Wholesale Distributors. And, FDA plans to pursue increased criminal penalties for counterfeiting in the United States Sentencing Commissions sentencing guidelines.

A. PRESCRIPTION DRUG MARKETING ACT (PDMA)

1) What FDA sought comment on:

- What are the most effective ways to achieve the goals of PDMA and, given recent or impending advances in technology discuss the feasibility of using an electronic pedigree in lieu of a paper pedigree?

2) What the Comments Said:

Many of the comments that discussed PDMA acknowledged the limitations and concerns of full implementation of PDMA. However, many comments also supported the use of paper pedigrees for their deterrent value and as a means to verify prior sales through due diligence. A risk-based approach to implementing PDMA, which focuses on those drugs that are at high risk of being counterfeited, was suggested, as well as maintaining a full pedigree that documents all sales and transactions back to the manufacturer for drugs and high risk. One comment suggested an interim solution of "one forward, one back" pedigree for high-risk drugs. However, a number of the comments noted the high cost and incomplete protection provided by such paper requirements, especially as a general interim measure; by the time these costly requirements were phased in, they could be replaced by a more modern system. A majority of the comments supported the eventual use of an electronic pedigree for all drug products in the supply chain and indicated that an electronic pedigree should be considered as a modern solution to fulfilling and exceeding the PDMA goals, and urged FDA to take steps to help achieve a reliable pedigree solution as quickly as possible. As noted above, FDA believes that substantial progress toward a more cost-effective

solution than incomplete and costly paper pedigrees is possible within the next several years. A detailed discussion of the comments is in Appendix B.

3) Discussion:

FDA has worked closely with affected parties to identify and resolve concerns related to the implementation of the pedigree requirements of the PDMA. Through the various public comment opportunities over the years, the agency has heard mixed reviews about the value, utility, and difficulty of implementing a paper pedigree that identifies each prior sale, purchase, or trade of such drug. The comments received in response to questions raised in the Interim Report confirm that these concerns continue.

FDA is encouraged by the enthusiasm and interest that stakeholders in the U.S. drug supply chain have expressed toward the adoption of sophisticated track and trace technologies that are more reliable than paper pedigrees. As discussed above, there appears to be movement by industry toward implementation of electronic track and trace capability in 2007. When this is in place, RFID should be able to function as a *de facto* electronic pedigree that follows the product from the place of manufacturer through the U.S. drug supply chain to the final dispenser. If developed properly, this electronic pedigree could be used to meet the statutory requirement in 21 U.S.C. § 353(e)(1)(A) to provide a pedigree under certain circumstances.

In the interim, until the electronic pedigree is in widespread use, voluntary adoption of multi-layer strategies and measures discussed in this report would reduce the likelihood that counterfeit drugs will be introduced into the U.S. drug distribution system. These measures, combined with RFID technology, can help provide effective long-term protections that will minimize the number of counterfeit drug products in the U.S. distribution system.

As discussed in a notice published in the Federal Register in conjunction with the publication of this report, FDA plans to continue to stay the of implementation of 21 CFR §§ 203.3(u) and 203.50. However, the agency intends to continue to reassess the stay of implementation on an annual basis. The agency will monitor closely whether progress toward the implementation of electronic pedigrees continues at the rapid pace evident in this task force analysis. Our plan to reassess the stay annually is part of the agency's strong commitment to see that effective product tracing is implemented as quickly as possible. The agency also encourages wholesalers to provide pedigree information that documents the prior history of a drug product, particularly for drugs most likely to be counterfeited, even when the passing of such a pedigree is not required by the Act. The suggestion from the comments that there be a one-forward, one-back pedigree for high-risk drugs in the interim, until an electronic pedigree is uniformly adopted, may have merit. However, FDA believes that Congress would have to amend section 503(e) of the Act if such a system is to become a requirement.

4) FDA Conclusion:

Adoption of electronic track and trace technology would help stakeholders meet and surpass the goals of PDMA. Therefore, FDA intends to focus its efforts on facilitating industry adoption of this technology within the next few years.

- To allow stakeholders to continue to move toward the goal of an electronic pedigree, FDA intends to delay the effective date of 21 CFR §§ 203.3(u) (definition of ADR criterion) and 203.50 (specific requirements regarding pedigree) until December 2006;
- By December 2006, FDA intends to determine whether to further stay the regulations or take other appropriate regulatory action.

B. MODEL RULES FOR WHOLESALE DISTRIBUTOR LICENSING STRENGTHENED

1) What FDA sought comment on:

- How should the NABP Model Rules for Licensure of Wholesale Distributors (Model Rules) be updated?
- Whether FDA regulations at 21 CFR Part 205, should be updated, as appropriate, to make it consistent with updates to the NABP Model Rules?

2) What the Comments Said:

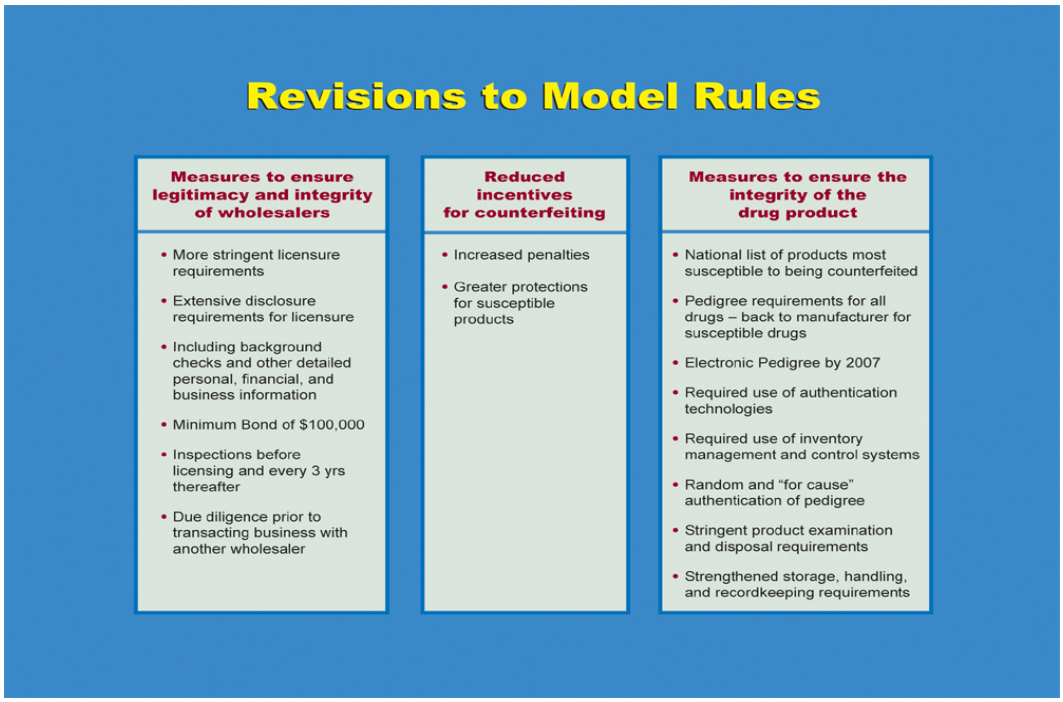
The comments overwhelmingly supported strengthening state requirements governing the licensure and oversight of wholesale distributors. Many comments cited the systemic weaknesses in the oversight of the wholesale drug industry and that existing inspection and due diligence processes are often insufficient to detect criminal activity. Some comments noted the positive steps already taken by some states, such as Florida, toward more effective regulation of wholesale distributors. For example, Florida has implemented more stringent requirements for licensure, stronger penalties, and due diligence requirements. Most comments stated that the full adoption of revised NABP model rules would improve security nationwide, and that stricter uniform standards were desirable across all 50 states so as not to create 50 different sets of criteria and rules for licensing. FDA was encouraged to revisit the current minimum standards requirements described in 21 CFR Part 205 to assess whether a 'federal floor' for states would enhance or diminish state efforts to meet the NABP recommendations. A detailed discussion of the comments is in Appendix B.

3) Discussion:

FDA is pleased to recognize the recent efforts by NABP in revising the Model Rules. The revised Model Rules significantly strengthen the requirements for licensure, as well as put in place or fortify requirements that will ensure and protect the integrity of drug products as they travel through the U.S. drug supply chain from the manufacturer to the consumer.

NABP sought comment from FDA, as well as interested stakeholders, in developing the revised Model Rules. The comments that FDA received as part of the anti-counterfeiting initiative have been discussed with NABP.

The revision of the Model Rules sought to enhance the protections included in the original version of the Model Rules and close existing gaps. The table below contains highlights of the revised Model Rules:



NABP is taking steps to facilitate implementation of the revised Model Rules, including: 1) publishing a list of susceptible products and calling for a coalition of national organizations to develop a process to maintain and update the list; 2) serving as bondholder for wholesalers in order to consolidate the need to hold a bond in all states where a wholesaler may do business; and 3) establishing a clearinghouse that will list wholesalers who receive accreditation by NABP and who have passed an inspection by their newly created inspection service, which NABP will conduct in partnership with the states. FDA supports NABP's efforts to facilitate adoption and implementation of the enhanced Model Rules.

Counterfeiting is a problem that is not isolated to one state. If a state strengthens its licensing requirements while a bordering state does not, the counterfeiters and illegitimate wholesalers will likely move into the bordering state. Widespread state adoption, implementation, and enforcement of the Model Rules would help combat counterfeiting.

4) FDA Conclusion:

Because States have an important role in regulating drug distributors, adopting and enforcing stronger state anti-counterfeiting requirements would help in our collective effort to detect and deter counterfeiting.

- FDA strongly supports the efforts taken by NABP to enhance the Model Rules and other actions taken to facilitate implementation;
- FDA supports all efforts by the States to adopt these Model Rules. Adoption of the model rules by all States would have a significant impact on protecting the nation's drug supply by ensuring that all persons and entities involved in wholesale distribution of drug products meet stringent licensing criteria and maintained high ethical and business standards;
- FDA encourages these state actions and the agency intends to explore whether and to what extent to revise the current minimum standards for state licensing of wholesale prescription drug distributors in 21 CFR Part 205.

C. HIGHER PENALTIES FOR DRUG COUNTERFEITING

1) What FDA sought comment on:

- Discuss the advantages and disadvantages of increased penalties for counterfeiting drugs

2) What the Comments Said:

There was overwhelming support and unanimous agreement that higher penalties for counterfeiting are needed.

3) Discussion:

FDA agrees with comments suggesting that higher penalties deter drug counterfeiters.

Current sentencing guidelines for counterfeit drug distribution are not commensurate with the public health threat posed by this criminal activity and

strengthening the guidelines should help deter such conduct in the first instance. Despite the significant threat to public health posed by counterfeit drug products, current law provides penalties far below the level of some purely economic crimes. For example, counterfeiting a prescription drug label (bearing a registered trademark) is punishable by up to ten years in prison, while counterfeiting the drug itself is punishable by a maximum of only three years in prison. Therefore, FDA plans to continue to pursue its request that the United States Sentencing Commission consider amending the sentencing guidelines to substantially increase criminal penalties for manufacturing and distributing counterfeit drug products and to specifically provide for enhanced penalties based on the level of risk to the public health involved in the offense.

4) FDA Conclusion:

FDA intends to pursue its request that the United States Sentencing Commission consider amending the sentencing guidelines to increase substantially criminal penalties for manufacturing and distributing counterfeit drugs and to provide specifically for enhanced penalties based on the level of risk to the public health involved in the offense.

3. CREATION OF A COUNTERFEIT ALERT NETWORK FOR INFORMATION DISSEMINATION AND EDUCATION

1) What FDA sought comment on:

- Whether a counterfeit alert network should be created through use of existing, or newly developed, communication tools, that allow reception, dissemination, and sharing of information about counterfeit drugs in a timely manner;
- What are the capabilities of current communication network, what a communication network should have in order to part of a counterfeit alert network, and costs associated with developing or adapting current systems.

2) What the Comments Said:

The agency received many comments supporting the creation of a counterfeit alert network. Most of the comments suggested that the agency take steps to build on existing networks and several comments offered their organizations' distribution lists or network as a conduit for the counterfeit alert network. The agency was advised that the counterfeit alert network should not be overused in order to avoid 'alert fatigue,' which could create indifference or doubt regarding the importance of the messages. The agency was encouraged to consider cost-

effective public/private partnerships to design communication strategies and facilitate efforts to standardize anti-counterfeit communications and to augment and coordinate communication systems. A detailed discussion of the comments is in Appendix B.

3) Discussion:

The FDA is committed to informing the public, particularly consumers, pharmacists, other health professionals, wholesalers, and others involved in the U.S. drug distribution system, about counterfeit drug incidents in a timely manner. FDA is also committed to educating them about ways to identify and prevent counterfeits from entering into this system. To increase awareness of counterfeit drugs and safeguard the nations drug supply, FDA is creating a network of national organizations, consumer groups, and industry representatives to deliver time-sensitive messages and information about specific counterfeit incidents and educational messages about counterfeits in general. The network is called the "Counterfeit Alert Network."

Partners in the Counterfeit Alert Network will be required to enter into a co-sponsorship agreement with FDA that lays out roles and responsibilities. Partners agree to disseminate the FDA time-sensitive messages to their members/subscribers/readers in the manner outlined in the co-sponsorship agreement, to partner in delivering educational messages, and in the case of health professionals, provide a link to the MedWatch website to report suspect counterfeits. A copy of the co-sponsorship agreement can be found in Appendix C.

The agency plans to maintain a list (as it does now) of additional health professional, consumer, and industry organizations, and media outlets to notify when an actual counterfeit incident is confirmed and what steps to take to minimize risks and remove the product from the U.S. distribution system. This will help ensure the widest possible distribution to the appropriate audience(s).

FDA met with consumer groups, pharmacy groups, and physician groups to determine the type of information that would be most useful to receive from FDA in the event of a counterfeiting incident. FDA intends to create templates for standardizing the format and content of health professional and consumer information in the event of a counterfeit incident that can guide outreach efforts in an efficient manner, while assuring the flexibility FDA needs to formulate the messages.

4) FDA Conclusions:

FDA will create a Counterfeit Alert Network that links together and enhances existing counterfeit notification systems, to provide for timely and effective notification to health professionals and consumers of a counterfeit event.

- FDA is creating a counterfeit alert network to partner with national healthcare organizations, consumer groups, and industry representatives to deliver time-sensitive messages about specific counterfeit incidents and educational messages about counterfeits in general, and information about how and when to report suspect counterfeit drug products;
- FDA plans to develop and execute multi-media informational strategies for specific audiences to ensure that the messages reach the largest number of interested people possible through the network;
- FDA plans to develop internal guidelines for the informational contents of outgoing FDA messages that will be most useful to communicate a counterfeiting incident to individual stakeholder groups.

4. HEALTH PROFESSIONAL REPORTING ENCOURAGED VIA MEDWATCH

1) What FDA sought comment on:

- Whether FDA's MedWatch system should be used as a tool to receive and disseminate timely information about counterfeit drug products, especially identification of suspect drug product?

2) What the Comments Said:

Most of the comments supported the use of MedWatch for reporting suspect counterfeit drugs. These comments stated that health professionals are familiar with MedWatch and it would be too cumbersome and expensive to develop a new system, which people would have to be educated to use. One comment believed that reports of possible counterfeiting should be separate from MedWatch because it is not designed for criminal activity reporting and oversight. Another comment stated that because MedWatch is a voluntary reporting system, there could be significant under-reporting.

3) Discussion:

For nearly ten years, MedWatch has been FDA's reporting portal for adverse drug reactions and 'product problems.' These include problems with product

quality that may occur during manufacturing, shipping, or storage, such as product contamination, defective components, poor packaging or product mix-up, questionable stability, and labeling concerns. If a pharmacist or consumer notices an unexplained change in size, shape, color, or taste of their dosage form, or notices that the coating is chipped or tablets are cracked, or that the drug is not working like it usually does, they may consider that to be a problem with their product. These are also characteristics that could occur if the product was a counterfeit drug. In fact, in the past, FDA has received some reports of suspect counterfeit drugs through MedWatch.

If a consumer suspects that his or her medicine is counterfeit, they are encouraged to contact the pharmacist who dispensed the drug, rather than report directly to MedWatch. The pharmacist may have information from the manufacturer that the shape, color, or taste of the product may have changed, or other information that may be helpful in determining if the product may be counterfeit or if the suspicious characteristic of the product or its packaging is expected.

The use of MedWatch is for health professional reporting. This would not affect the agreement with the Pharmaceutical Research and Manufacturers of America (PhRMA), whereby manufacturers have agreed to report counterfeits of their products to FDA's Office of Criminal Investigations, within 5 days of becoming aware of the counterfeit.

FDA has streamlined procedures for processing reports of suspect counterfeit drugs. The MedWatch Central Triage Unit (CTU) standard operating procedures (SOPs) have been amended to include "suspect counterfeit product" as a category of reports, so the CTU will know where to send the report for expedited processing.

It is easy and convenient to file a report with MedWatch. All reports are confidential and the identity of the reporter is not disclosed. FDA encourages reporting using the online reporting form that can be found at www.fda.gov/medwatch .

4) FDA Conclusion:

FDA plans to encourage and educate health professionals to report suspect counterfeit drugs to MedWatch.

- FDA plans to encourage and educate health professionals to report suspect counterfeit drugs to MedWatch as an overarching mechanism to report such information;
- FDA plans to change the instructions for the MedWatch reporting form, both paper and online versions, so reporters will know how and when to report suspect counterfeits. Additionally, FDA plans to

amend the MedWatch website description of product problems to include suspect counterfeits.

Change made to the instructions on the MedWatch reporting form.

5. SECURE BUSINESS PRACTICES

1) What FDA sought comment on:

- Whether to develop sets of "secure business practices" which would be voluntarily adopted by manufacturers, wholesalers, re-packagers, and pharmacies?
- Whether stakeholders should designate an individual or team to coordinate security and anti-counterfeiting activities?
- Issuance of an FDA guidance document concerning physical site security and supply chain integrity?
- There was no proposal specific to re-packagers. However, FDA identified independent re-packaging operations, through several ongoing investigations, as a point of entry for counterfeit drugs into the distribution system, and some of the proposed options would have had the effect of limiting those re-packaging operations.

2) What the comments said:

The comments supported the need for development of secure business practices by all stakeholders in the drug distribution chain because each stakeholder has a responsibility to ensure that pharmaceutical products are authentic. The

comments suggested that such practices include ensuring the legitimacy of business partners and refusing to do business with persons of unknown or dubious background, taking steps to ensure physical security, and identifying an individual or team in the organization with primary responsibility for ensuring that effective security practices are implemented.

It is critically important that the physical facilities involved in the production, distribution, or dispensing of pharmaceuticals are secure against counterfeit drugs. In the area of food safety, our Center for Food Safety and Nutrition (CFSAN) has issued guidance for the food industry on preventive measures that establishments may take to minimize the risk that products under their control will be subject to tampering or other malicious, criminal, or terrorist actions.

Although it was acknowledged that re-packagers were required to comply with Current Good Manufacturing Practices as set forth in 21 CFR 210 and 21 CFR 211, due to the involvement of re-packaging operations in some recent counterfeiting schemes, FDA was asked to provide more oversight and to conduct more frequent inspections of re-packagers.

See Appendix B for a detailed discussion of actions taken by manufacturers, wholesalers, and pharmacists to develop secure business practices.

3) Discussion:

Recent counterfeiting cases demonstrate that the current business practices of participants in the U. S. drug distribution system are in some cases inadequate to prevent the introduction of counterfeit drugs. Implementation of secure business practices by participants in the U.S. drug supply chain is critical for deterring and detecting counterfeit drugs. Therefore, FDA commends and strongly supports efforts to develop and implement secure business practices for these participants. FDA plans to facilitate and encourage the development of innovative approaches to securing business transactions in the drug supply chain. The number of stakeholders who have told FDA they are already implementing the business practices discussed above is very encouraging. In addition to identifying effective security measures, the designation of an individual or team to have primary responsibility for coordinating security activities helps ensure effective implementation.

FDA agrees that re-packaging operations can be a significant vulnerability in the drug supply chain. Although current statutory and regulatory requirements allow for appropriate oversight of re-packagers, FDA agrees that enforcement of those requirements could be strengthened.

4) FDA Conclusions:

For government efforts against counterfeit drugs to be successful, drug producers, distributors, and dispensers will have to take effective actions to secure their business practices.

- Efforts by stakeholders to develop the secure business practices listed above would help protect the public health and diminish counterfeiting;
- FDA plans to work with individual stakeholders and groups representing stakeholders, as necessary and appropriate, to continue to develop, make publicly available, and widely disseminate secure business practices;
- Good security practices include designation of an individual or team, reporting directly to the organization's senior management, to coordinate the security and anti-counterfeiting activities for the organization;
- FDA supports efforts by pharmaceutical manufacturers, wholesalers, and retailers to secure their physical facilities against counterfeit drugs. FDA plans to issue guidance on physical site security that applies to participants in the U.S. drug distribution system.
- FDA plans to make its oversight over re-packagers of drugs a higher priority. FDA expects to increase the frequency with which it inspects re-packagers whose operations are found to be at increased risk for the introduction of counterfeit drugs. The increase in frequency will be based on the degree of risk, as determined by applying to re-packaging operations the risk based model FDA is developing for prioritizing inspections of drug manufacturing sites.

6. FDA'S RAPID RESPONSE TO REPORTS OF SUSPECT COUNTERFEIT DRUGS STREAMLINED

1) What FDA sought comment on:

- Enhancing FDA's internal processes for responding to and investigating reports of suspected counterfeit products

2) What the Comments Said:

The comments unanimously supported any efforts by the agency to rapidly respond to reports of suspect counterfeit drugs.

3) Discussion:

FDA takes reports of suspect counterfeit products very seriously. The agency is proud of its investigative tools and talents and its quick response to the public health needs when a counterfeit has been reported and has been confirmed. To improve this process, the agency evaluated its policies and procedures for responding to reports of counterfeit drugs to determine if FDA's response could

be more efficient. Although FDA has had many positive experiences in responding and working with manufacturers and the public, FDA identified several ways to further enhance coordination and communication among all initial responders within the agency.

Because different parts of the agency throughout the country may receive the potential counterfeiting report, in some instances, it may take time for the information to flow to the appropriate people who need it to respond efficiently. Therefore, FDA has established an FDA-wide rapid response protocol for suspect counterfeit drugs that will ensure that specified persons/offices/divisions within the agency are notified and engaged as soon as possible after the report is made to the agency. Policies and procedures have been or will be amended to reflect this streamlined information flow and coordination of agency response. Increased coordination and communication will help FDA to initiate rapidly any criminal or civil investigation, as well as to assess the health hazard of the counterfeit situation so the public health response can be launched.

4) FDA Conclusion:

To respond rapidly to a report of a suspect counterfeit, FDA is further streamlining its internal processes to respond quickly to reports of suspect counterfeit drugs by improving coordination and communication among all initial responders in the agency.

- FDA intends to amend its internal SOPs, where appropriate, to provide for more rapid response when a suspect counterfeit is reported;
- FDA intends to build on lessons learned from working with manufacturers in past counterfeiting experiences to determine how industry/agency collaboration can and should be strengthened.

7. EDUCATING THE PUBLIC AND HEALTH PROFESSIONALS

a. Consumers

1) What FDA sought comment on:

- As the sophistication of the "final product" drug counterfeiting operations has increased, the public needs to be more aware of ways to identify the risk of counterfeit drugs, receive instructions on ways to minimize the chance of receiving fake products and to identify potential counterfeits.

2) What comments said:

The comments stated that it is imperative that consumers be encouraged to be more proactive in managing their health and be given useful tools to be vigilant to help avoid potential counterfeit drugs. Consumers should be educated to be aware of noticeable differences in their medication, the packaging, or any adverse events. In addition, consumers should understand the important role that their pharmacist and healthcare providers can play in identifying, reporting, and responding to counterfeit drug events. However, the comments warned that care should be taken in any education campaign to not unnecessarily alarm the public.

3) Discussion:

Despite the growing sophistication of counterfeit drug threats, many consumers are not fully aware of these risks. The Agency, in conjunction with consumer and patient advocates, as well as industry representatives is eager to find additional creative ways to educate the public of the potential threat of counterfeit drugs. The messages should alert consumers to the risk, offer ways consumers can recognize the signs of a potentially counterfeit product, teach them how to reduce the risk of exposure and tell them what to do if they suspect they have encountered one. Of course, FDA wants to strike an appropriate balance in the need to proactively educate consumers without causing unnecessary alarm that could interfere with their use of prescribed drug regimes. Most important, it is critical to focus awareness, and education programs should focus on issues that consumers can control.

FDA has an ongoing educational campaign that is intended to educate consumers about the risks of buying medicines online. FDA intends to reaffirm this message and focus the educational campaign on teaching safe purchasing methods. Particular focus will be placed on encouraging the public to seek out the Verified Internet Pharmacy Practice Site (VIPPS) seal when purchasing from an online pharmacy.

In addition, stakeholders indicated that there is a need for better, timelier, accurate information about specific counterfeit situations. FDA plans to create a counterfeit drug resource page on our website. The objective of this webpage is to concentrate customized education tools into a resource library that can empower individual stakeholder groups.

4) FDA Conclusions:

Educating the consumers about the risks of counterfeits is a critical piece in the effort to stop counterfeits from entering the stream of commerce.

- FDA plans to develop additional, multi-layer, consumer-oriented educational materials that will help them learn about counterfeits, what to watch for, and where to turn for useful information if they think they have encountered a suspected counterfeit;
- FDA plans to re-launch the FDA public service announcement (PSA) campaign for best online buying practices to educate consumers about how to buy drugs online safely, and risks to avoid in online purchasing;
- FDA plans to house on its www.fda.gov website a comprehensive, consumer-friendly online library that will contain both general and specific counterfeit drug information. It will also contain targeted educational materials for various interest groups that discuss counterfeit issues generally. In addition, the agency intends to develop a new FDA anti-counterfeiting resources icon to increase familiarity with the issue.

b. Pharmacists and Other Health Care Professionals

1) What FDA sought comment on:

- Pharmacists need improved tools to receive information and to educate themselves about how to handle these situations and to keep abreast of current counterfeit events. They need to know how to identify and counsel consumers who might have received counterfeit products.
- Physicians, nurses and other health professionals also have contact with consumers taking pharmaceuticals and can help identify and counsel patients that could have accessed a counterfeit. This will require these groups keep up to date on current counterfeit events and know steps to take to report situations if a counterfeit is suspected.

2) What the comments said:

Groups representing pharmacists and pharmacies recognize the need for pharmacists to take a leadership role in the identification of counterfeits, prevention of their introduction into the distribution chain, and education of consumers about counterfeits.

The healthcare community indicated that awareness and education campaigns are important if its health professionals are to be active participants in the fight against counterfeit drugs.

3) Discussion:

Pharmacists and health professionals can play a major role in helping identify counterfeits and preventing their introduction into the distribution chain. FDA has been working with pharmacy and medical professional groups to develop

educational materials for pharmacists and other healthcare professionals, including doctors, nurses, and physician assistants.

4) FDA Conclusion:

FDA plans to enhance its educational programs for pharmacists and other heath professionals about their role in minimizing exposure to, identifying, and reporting counterfeits.

- FDA intends to work with pharmacy and health care professional groups to develop materials to help educate their profession on the risk of counterfeits, what to do in case a counterfeit is suspected and ways to aid in educating consumers. This will include development of clear, concise messages and protocols, as well as the establishment of a delivery mechanisms that will help them learn about the threat of counterfeits, what to watch for, and where to turn for useful information in the case of a suspected counterfeit;
- FDA intends to encourage pharmacy and health care professionals to become partners in the agency's newly established Counterfeit Alert Network;
- FDA intends to expand its outreach efforts by presenting at or participating in conferences and by publishing articles in professional journals and periodicals that target audiences of doctors, nurses, pharmacist and hospital administrators to educate them about counterfeits and raise awareness of the risks;
- FDA intends to work with health professional trade groups to identify or improve data collection/ reporting systems that could help identify counterfeits as they enter the stream of commerce (i.e., include appropriate questions on the ER patient admission questionnaire that might help diagnose usage of a counterfeit drug,)

8. INTERNATIONAL APPROACH

1) What FDA sought comment on:

- Strengthening international cooperation in law enforcement efforts, identifying counterfeit products, using anti-counterfeiting technologies, and educating stakeholders and consumers
- Whether there should be global standards for packaging of pharmaceuticals and the use of anti-counterfeiting technologies

2) What the comments said:

The comments supported FDA involvement in global efforts to deter and detect counterfeit drugs.

3) Discussion:

The growing global prevalence of counterfeit drugs must be curtailed. The steps described in this report are intended to secure the U.S. domestic drug supply. However, as long as counterfeit drugs exist worldwide, opportunities could arise for counterfeit drugs to find their way into the U.S. Many countries have taken steps to secure their nation's drugs supply, while others struggle because of limited resources, inadequate regulatory infrastructure, or competing national health priorities. The World Health Organization (WHO) has taken the lead to increase worldwide collaboration and to develop strategies to deter and detect counterfeit drugs. There are several international criminal enforcement collaborations, such as the Permanent Forum on International Pharmaceutical Crime and the Interpol Intellectual Property Crimes Action Group. FDA intends to work with WHO and other international organizations to develop and implement worldwide strategies to combat counterfeit drugs.

4) FDA Conclusions:

FDA will collaborate with foreign stakeholders to develop strategies to deter and detect counterfeit drugs globally.

Below is a table showing when certain anti-counterfeiting measures will be available:

APPENDICES

Appendix A: Counterfeit Alert Network Co-sponsorship Agreement
Appendix B: More detailed description of the comments received for certain issues (where the comments were diverse or lengthy)

APPENDIX A

COUNTERFEIT ALERT NETWORK CO-SPONSORSHIP AGREEMENT

BACKGROUND

The U.S. Food and Drug Administration (FDA) is committed to informing the public, particularly consumers, pharmacists, other health care professionals, wholesalers, and others involved in the U.S. drug distribution system, about counterfeit drug incidents in a timely manner and educating these parties on ways to identify and prevent counterfeits from entering into this system. To increase awareness of counterfeit drugs and safeguard the nations drug supply, FDA will create a network of national organizations, consumer groups, and industry representatives to deliver time-sensitive messages and information about specific counterfeit incidents and educational messages about counterfeits in general. FDA also will develop and execute informational strategies for specific audiences to ensure that the messages reach the largest number of interested people possible through the network. The network will be called the "Counterfeit Alert Network."

The goals of the Counterfeit Alert Network include, but are not limited to:

disseminating alert messages to a wide audience about specific counterfeit drug incidents in the U.S. and measures to take to minimize exposure (e.g., recall information);

outlining the roles and responsibilities of consumers, pharmacists, other health professionals, and wholesalers must play to identify counterfeit drugs, report suspect counterfeit drugs, and prevent them from entering the U.S. distribution system; and

developing a network of national organizations, consumer groups, and industry representatives to help disseminate the information.

[INSERT CO-SPONSOR ORGANIZATION INFORMATION]

IMPORTANCE OF THE PARTNERSHIP TO FDA AND [ORGANIZATION]

This partnership will increase the potential audience of FDA's important notifications about specific counterfeit drug incidents and messages about how and when to report suspect counterfeit drugs. By distributing FDA-developed messages through the [ORGANIZATION] information system, these messages can reach more than [#] people.

RESPONSIBILITIES OF FDA AND [ORGANIZATION]

FDA will develop targeted messages, with a particular focus on consumers, pharmacists, and other health care professionals when a counterfeit drug is found in the U.S. distribution system. FDA will also develop educational and informational materials about how to detect a counterfeit drug, what to do if a drug is believed to be counterfeit, how to report the suspect counterfeit to the FDA, and ways to minimize the risk of receiving a counterfeit drug. These materials may include: web-based documents, print ads, posters, prepared newspaper articles, fact sheets, consumer brochures/pamphlets, and informational packets. FDA will provide any logistical and technical support, such as writing, layout, designing, and preparing illustrations for the products.

FDA will ensure that all materials are cleared through the Agency and the U.S. Department of Health and Human Services before releasing material to the [ORGANIZATION] for public distribution FDA will provide these materials in a format (hard copy, digital, or electronic) that [ORGANIZATION] can use, as appropriate, to create, manufacture, and/or have printed in enough quantities to distribute to various audiences. FDA will not be responsible for any costs outside of the materials already produced by FDA.

[ORGANIZATION] will distribute in a timely manner FDA's notifications about specific counterfeit incidents as an alert through an active messaging system (separate email or fax alert correspondence). [ORGANIZATION] will facilitate the ability of their members/subscribers/website visitors to report suspect counterfeit drug products to FDA, e.g., via a link to the FDA Counterfeit Drugs webpage or FDA's MedWatch webpage. [ORGANIZATION] will distribute relevant FDA - educational messages about counterfeits, covering such issues as awareness, recognition, prevention, tracking, and authentication of drug products.

The [ORGANIZATION] will pay for the cost, if any, of printing materials, posting materials on its website, email distribution, renting ad space, and securing print placement in magazines and newspapers, as appropriate. [ORGANIZATION] will make clear, in any solicitation for funds to cover its share of the distribution costs that it, not FDA, is asking for the funds. [ORGANIZATION] will not imply that FDA endorses any fundraising activities in connection with the event. [ORANIZATION] will make clear to donors that any gift will go solely toward defraying the expenses of [ORGANIZATION], not FDA.

FDA and the [ORGANIZATION] will develop a dissemination plan that outlines where and how the educational materials and alert messages about specific counterfeit incidents will be distributed to various audiences.

FDA and the [ORGANIZATION] will review this agreement in two (2) years from the original date of this agreement, but either party to this agreement can

terminate its participation at any time by notifying the other party of its intent to do so in writing.

CHARGES
The [ORGANIZATION] will not sell any educational materials related to this joint effort. [ORGANIZATION] will not impose an enrollment or registration fee for subscribers to receive this information.

INDEPENDENTLY SPONSORED PORTIONS AND ENDORSEMENTS
All materials and efforts related to the Counterfeit Alert Network will be jointly sponsored. FDA staff will not be used to develop, promote, or otherwise support any event that is independently sponsored by the co-sponsor, although official announcements and brochures may contain factual references to the available materials and Counterfeit Alert Network messages.

The [ORGANIZATION] will not use the name or logo of FDA except in factual publicity. Factual publicity includes materials provided to [ORGANIZATION] on FDA's program and Counterfeit Alert Network materials. Such factual publicity shall not imply that the involvement of FDA serves as an endorsement of the general policies, activities, or products of the [ORGANIZATION]. Where confusion could result, a disclaimer should accompany publicity to the effect that no endorsement is intended. The [ORGANIZATION] will clear all publicity materials with FDA to ensure compliance.

RECORDS
Records concerning this partnership shall account fully and accurately for any financial commitments and expenditures of FDA and [ORGANIZATION]. Such records shall reflect, at a minimum, the amounts, sources, and uses of all funds.

PUBLIC AVAILABILITY
This co-sponsorship agreement, as well as any financial records for this partnership, shall be publicly available.

CO-SPONSORSHIP GUIDANCE

FDA and the [ORGANIZATION] will abide by the memorandum of August 8, 2002, "Co-sponsorship Guidance," issued by the Associate General Counsel for Ethics.

_____ _____

DATE

FDA Signee

_____ _____

[NAME] DATE
[TITLE]
[ORGANIZATION]

_____ _____

Director, Ethics and Integrity Staff DATE
Office of Management and Programs
Office of Management
Food and Drug Administration

APPENDIX B

EXPANDED DESCRIPTION OF COMMENTS RECEIVED

TECHNOLOGY

Unit of Use Packaging

Comments supporting widespread utilization of unit of use technology cited:

- The decreased need for repackaging which is a point of entry for counterfeit drugs;
- Authentication technologies applied by the manufacturer would reach the dispensing pharmacy and the patient;
- The lower cost for utilizing unit of use packaging on newly approved drugs;
- The deterrent value to counterfeiters of the higher costs of duplicating unit of use packages;
- Improvement in patient safety due to reduction in dispensing errors and better patient compliance; and
- Increased pharmacist availability for patient counseling (due to reduction in time needed to fill prescriptions).

Some comments cautioned the FDA against mandating unit of use packaging for all drugs citing:

- The high cost, and length of time, it would take to change production lines from bulk to unit of use packaging;
- The investment made by many pharmacies in re-packaging and pill counting equipment;
- The difficulty of packaging certain products (e. g. vaccines, multi-dose liquid formulations) in unit of use form;
- The need to differentiate repackaging performed under contract to a manufacturer or by a pharmacy (which may achieve market efficiencies) from repackaging by other entities;
- The need to perform a careful product-by-product cost-benefit analysis on unit of use packaging before creating any requirements;
- The minimal hurdle that unit of use packaging creates for sophisticated drug counterfeiters;
- The need to comply with the Consumer Product Safety Commission (CPSC) regulatory requirements for child resistant unit of use packaging;
- The difficulty some consumers (e.g., arthritic patients) may have in opening unit of use packaging such as some blister packs;
- The need for pharmacists to modify prescribed quantities to correspond with available unit of use packages which could require changes in state law; and

- The need to establish standards for such things as size and shape of unit of use packaging in order to minimize patient confusion and address shelf space issues.

Authentication Technologies

They supported use of authentication technologies as part of an overall anti-counterfeiting strategy and stated that authentication technologies serve two purposes:

They make it more difficult and expensive to produce a copy of the drug or its packaging and labeling, and
They provide a means for determining if a specific drug, package, or label is authentic.

Manufacturers of specific anti-counterfeiting technologies provided us with descriptions of their products that were extremely valuable in helping us understand how they work, their cost, and how they might be incorporated into pharmaceutical products, packaging, and labeling or used to detect counterfeit products through forensic and other analytical methods, including rapid methods.

Many comments supported the issuance of an FDA guidance document on the use of authentication technologies. They stated that there was no clear FDA policy specifically targeted to this important subject. They suggested that current FDA policies and practices for New Drug Applications (NDAs), Abbreviated New Drug Applications (ANDAs), and Biologics License Applications (BLAs), supplements, and other notification procedures should be clarified so the policies and procedures applicable to use of anti-counterfeiting technologies are clearly articulated and available in a single document.

The following points were made regarding the use of authentication technologies on drug products, their packaging and labeling:

- There is no “silver bullet” solution – all anti-counterfeiting technologies can be defeated;
- Because all anti-counterfeiting technologies can be defeated, a more extensive approach utilizing layered overt and covert technologies that are changed on a regular basis is frequently required;
- Authentication technologies are expensive;
- Manufacturers should determine which authentication technologies to use, on a product specific basis. The FDA should not require the use of any specific anti-counterfeiting technology. For example: the number and type (e.g., overt, covert) of technologies utilized for a given product need to take into account the type of product (e.g., solid, liquid), use, cost, history of counterfeiting etc.;

- Repackaging destroys anti-counterfeiting technologies employed by the manufacturer;
- Incorporation of anti-counterfeiting measures into the product, packaging, and labeling may be subject to application and notification requirements which means that initiating or changing such technology could require a significant time and expense;
- Although all products are at risk for being counterfeited there is a need to develop criteria or a classification system to help identify those products at highest risk for being counterfeited and thereby assist stakeholders in identifying products that might derive a greater benefit from the incorporation of authentication technologies;
- The large number of available technologies coupled with the number of different products stocked in pharmacies and the need to change anti-counterfeiting measures make it difficult for pharmacists to be knowledgeable about the technologies used for a product at any given time;
- Technologies that do not allow for "real time" or consumer authentication (e. g., covert technologies known only to the manufacturer and/or the FDA) may have an uncertain benefit in rapid identification of counterfeit drugs.

List of Drugs Likely to be Counterfeited

Many comments stated that it was important for stakeholders to allocate financial resources to protect those products that are most likely to be counterfeited. There was agreement that the criteria we suggested to identify drugs that were likely to be counterfeited were correct. These included:

- Impact on public health if the drug were counterfeited;
- Drugs history of counterfeiting;
- Drugs price;
- Drugs volume;
- Drugs dosage form;
- Drugs clinical uses; and
- Whether similar products had a history of being counterfeited.

However, there was no consensus on how to apply these, or other, criteria in creating a list of such products.

As stated above, some comments suggested that instead of developing a list of drugs likely to be counterfeited, a set of criteria for determining whether a drug was at likely to be counterfeited should be created. One proposal for such criteria was:

A drug has been subjected to a seizure or stop sale notice because of counterfeiting, or

There is documentation that a drug was counterfeited and is the subject of an investigation by federal or state authorities
AND
The product is high cost (e.g., over $200 per dose) or high volume (e.g., top fifty drugs), or
The product is used extensively for treatment of HIV/AIDS or cancer, or
The product is injectable, or
The product distributed in a special or limited way, or
There are multiple documented instances of pedigrees not being passed with the product

Radiofrequency Identification Technology

We received a large amount of information on the benefits, costs, and unresolved issues relating to RFID. These include:

Benefits

- Ability to deter and detect counterfeit drugs;
- Ability to conduct efficient targeted recalls;
- Ability to manage inventory;
- Ability to identify theft;
- Ability to identify diverted drugs; and
- Improvement in patient safety by assuring correct dispensing of drugs.

Costs

- Purchasing hardware (e.g., tags, readers) and software;
- Integration into legacy information systems;
- Database creation, security, and maintenance;
- Integration of RFID technology into existing manufacturing processes, distribution procedures;
- Compliance with regulatory requirements (e.g., cGMP, notification, product integrity); and
- Feasibility studies.

Unresolved Issues

- Need for all stakeholders to embrace the technology in similar timeframes in order to realize the full potential of RFID technology including provision of a universal electronic pedigree;
- Need to develop standards and business rules;
- Need to address database issues such as structure (e.g., central vs. distributive), ownership, access, and security;
- Clarification of regulatory requirements pertaining to use of RFID (e.g., cGMP, electronic records, notification); and

- Need for a flexible migration path to the use of RFID in order to meet the needs of different stakeholders.

Stakeholder Activities

We have been informed of several feasibility studies, starting in early 2004, that should give members of the supply chain experience using RFID as well as provide them with an opportunity to test its business uses and identify potential barriers to its acceptance. These studies include:

- Wal-Mart: drug manufacturers and wholesalers will attach RFID tags to all bottles of controlled substances;
- Accenture: coordinating a study of RFID involving manufacturers, wholesalers, and retailers that will explore the use of RFID for tracking, tracing, recalls and theft of selected pharmaceuticals;
- CVS: is studying the potential benefits that tagging and tracing pharmaceuticals and prescriptions in a retail pharmacy would have on operating efficiency, quality of patient care, and customer service; and
- Other feasibility studies using RFID are being planned in Europe to study the use of serialization for authentication at the point of dispensing.

In addition to feasibility studies, we understand that several groups representing many supply chain participants have been meeting to discuss ways to facilitate the adoption of RFID. For example the Product Safety Task Force (PSTF) convened under the auspices of the Healthcare Distribution Management Association (HDMA) is developing business requirements and identifying business issues relating to RFID technology.

The PSTF and other stakeholders have informed us that the migratory path (or phase in) to widespread use of RFID at a package level could vary by stakeholder based on the place of that stakeholder in the supply chain (e.g., manufacturer vs. retailer) and on specific costs and benefits accruing to that stakeholder (e.g., types of products manufactured, number of distribution centers, technology cost per product).

Several migratory paths were mentioned, including:

- Phasing in use of RFID technology with use at the case and pallet preceding use at the package level;
- Phasing in use of RFID technology starting with use on pallets, cases, and packages of “high risk” products with gradual inclusion of other products at all levels; and
- Use of RFID technology at the pallet and case level coupled with use of 2-D Bar Codes at the package level with gradual phase in of RFID technology at the package level.

According to stakeholders, these paths are not mutually exclusive and it is likely all of these, and other, paths will be utilized as RFID technology becomes more widely adopted.

SECURE BUSINESS PRACTICES

Below are some of the secure business practices that have been developed by participants in the U. S. drug distribution system.

Manufacturers

Several manufacturers have announced policies intended to secure the supply chain. These policies include:

- Limiting sales to authorized wholesalers. Authorized wholesalers are defined either as wholesalers who purchase a manufacturers products exclusively from that manufacturer or as wholesalers who purchase a manufacturers product directly from the manufacturer or from other authorized wholesalers;
- Making the list of authorized distributors publicly available;
- Ability to audit the sales records of wholesale distributors;
- Working with dispensing pharmacies to ensure they are aware of the identities of authorized distributors; and
- Designation of an individual or team to coordinate security and anti-counterfeiting activities.

Wholesalers

The Healthcare Distribution Management Association (HDMA) released a document entitled *"Recommended Guidelines for Pharmaceutical Distribution System Integrity"* which set forth a series of recommended actions for wholesalers to take prior to and while conducting business transactions with other wholesalers. In essence they comprise a "due diligence" checklist which includes items such as:

- Obtaining detailed information about the wholesalers licensure, inspection results, history of disciplinary actions, corporate officers, owners, and management personnel;
- Performing a criminal background check on the wholesaler, its officers, owners, and other key personnel;
- Obtaining a credit history and information about its business activities, financial status, and liability insurance;
- Performing a detailed physical site inspection; and

- Ensure that the wholesaler is in compliance with federal and state requirements, verifies that the wholesaler is an authorized distributor for the products being transferred or has a process in place for verifying pedigrees.

Individual wholesalers supported the HDMA guidelines and provided FDA with ideas for additional secure business practices including:

- Not selling pharmaceuticals to other wholesalers at all; and
- Completely separating the functions of quality assurance and compliance from sales and marketing and requiring quality assurance and compliance staff to perform due diligence on potential business partners.

Pharmacies and Pharmacists

We have been informed that several organizations representing pharmacies and pharmacists are developing secure business practices as a guide for pharmacies and pharmacists. One pharmacy group notified us that they have already published a list of strategies to use for assuring the integrity of pharmaceuticals. This list includes:

- Staying informed about reports of counterfeit drugs;
- Contacting wholesalers to get information about the status of their licensure, whether they are authorized distributors, and where they source their drugs;
- Evaluate pharmacy security;
- Educate hospital staff;
- Follow up on patient complaints; and
- Report suspect products.

PRESCRIPTION DRUG MARKETING ACT (PDMA)

A majority of the comments that discussed PDMA noted the limitations and concerns of full implementation of PDMA. Such limitations include:

- Paper pedigrees can be forged and counterfeited;
- Paper pedigrees are logistically difficult to accommodate in the drug distribution system;
- ADRs are not required to pass pedigree information on to the next purchaser, so subsequent wholesalers are unable to obtain the pedigrees needed to sell their products;
- The pedigree for a product that circulates several times through the supply chain loses all prior sales history if the drug product is sold to an ADR;
- The net effect is that secondary wholesalers who cannot obtain pedigrees necessary to legally market drugs could be driven out of business;

reducing the number of legitimate distributors in the system, decreasing competition and increasing prices;
- Manufacturers do not update their lists of ADRs so it is difficult for a wholesaler to obtain ADR status; and
- Costs of paper pedigrees outweigh the benefits.

A number of other comments, however, supported the use of paper pedigrees for their deterrent value and as a means to verify prior sales through due diligence. Comments noted that even forged pedigree papers provide an additional opportunity to identify counterfeiters and block introduction of counterfeit drugs into the drug supply if wholesalers exercise due diligence by tracing the sales through the pedigree and identifying the place where the forgery occurred. A few comments suggested that FDA should exercise enforcement discretion and not take enforcement action against a wholesaler who fails to provide pedigree information back to the manufacturer as long as the wholesaler provides pedigree information back to the first ADR who received the drug from the manufacturer.

Several comments suggested a risk-based approach to implementation of the PDMA, which focuses on those drugs that are at high-risk of being counterfeited. Many of these comments suggested that high-risk drugs maintain a full pedigree that documents all sales and transactions back to the manufacturer. One comment suggested an interim solution of "one forward, one back" pedigree for high-risk drugs. This system would be analogous to recent bioterrorism legislation for food distributors, whereby participants in the food distribution system maintain only those records necessary to identify immediate previous sources and immediate subsequent recipients of food. However, comments on FDA's food regulations have suggested it will take at least several years to phase in the paper recordkeeping requirements. Moreover, in contrast to drugs, there are no major steps in development now to provide widespread electronic pedigrees for drug products. Finally, as noted throughout the riskiest drug products are the ones for which modern anti-counterfeiting and track-and-trace methods should be implemented soonest.

Most comments supported the development of an electronic pedigree for all drug products in the supply chain and that an electronic pedigree should be considered as a long-term solution to fulfilling the PDMA requirements codified at 21 CFR 203.50. Given the costs of implementing the partial anti-counterfeiting measures included in the PDMA, and the expectation of continued significant progress toward implementation of modern pedigree systems for drugs, more effective modern pedigree systems are likely to be available before it would be possible to phase in and achieve compliance with paper pedigree requirements.

MODEL RULES FOR WHOLESALE DISTRIBUTOR LICENSING

The comments overwhelmingly supported strengthening requirements governing the licensure and oversight of wholesale distributors. Many comments cited the systemic weaknesses in the oversight of the wholesale drug industry, prior to Florida's implementation of licensing reform, that were described in the Florida Grand Jury Report, such as issuing licenses without proper background checks and granting licenses despite one or more felony convictions. The comments also stated that existing inspection and due diligence processes are often insufficient to detect criminal activity. As mentioned above, there was uniform agreement that the penalties for counterfeiting drugs are insufficient to serve as an adequate deterrent.

Many comments supported the concept of tighter requirements generally, while others gave specific suggestions for improvement. Some of the specific suggestions included:

- Detailed and robust applications that provide greater disclosure of information about the applicant and their prior history;
- Criminal background checks for applicant and company principals;
- List of prescription drug-related or fraud- related activities that are "not in the public interest" such that states should deny licenses to persons with criminal records for these activities;
- Pre-license inspection of wholesale distribution facilities;
- Periodic and unannounced inspections;
- National clearinghouse for information on wholesale licensure status, debarments, exclusions, and/or results of criminal background checks;
- Bonds of up to $100,000;
- Requiring all wholesalers to transmit pedigree tracing transactions back to the manufacturer for susceptible products;
- Non-ADRs must pass pedigree with all drugs with transaction information back to an authorized distributor;
- Amending the definition of ADR to include those on the manufacturers list, have a written agreement currently in effect with the manufacturer, or has a verifiable account with the manufacturer and minimal transactional or volume requirement thresholds from the manufacturer of 5000 sales units within 12 months or 12 purchases (invoices) within 12 months;
- Requiring authentication of pedigree if there is reason to suspect that the product may be counterfeit, as well as on a random basis;
- Migrating to electronic pedigree;
- More aggressive penalties and enforcement on state and national level;
- Quickly suspending and/or revoking licenses of violators; and
- Including due diligence requirements for wholesalers to conduct on its suppliers.

Most comments stated that the stricter standards should be uniform across all 50 states so as not to create 50 different sets of criteria and rules for licensing.

Concerns about several provisions in the new Florida and Nevada laws regarding licensing of wholesale distributors were expressed. Some of the comments described implementation and logistical problems that wholesalers have experienced in these states as a result of the new law.

Some comments encouraged FDA to revisit the minimum standards requirements described in 21 CFR Part 205 to create a 'federal floor' for States to meet. The comments were not uniform, however, on whether such a federal floor might enhance or deter state efforts to implement the complete set of NABP recommendations.

COUNTERFEIT ALERT NETWORK FOR INFORMATION DISSEMINATION AND EDUCATION

The agency received many supportive comments about the counterfeit alert network concept. Most of the comments suggested that the agency use existing networks and several comments offered their organizations distribution list or network as a conduit for the counterfeit alert network.

Some comments offered strategic approaches for the development of such a network, including suggested concepts for message delivery. Suggestions include using active notification via "push" email technology, validated and secure systems, easily understood language with clear and unambiguous messages, multiple notification systems, accessible to all stakeholders, no cost for users, timely, visual alert to flag importance, redundant delivery vehicles such as email, fax, direct mail, and phone, and have an embedded link to take user back to FDA or MedWatch website. The comments also suggested that consistency is an important element so there is familiarity in times of emergency situations. The agency was warned not to overuse the counterfeit alert network in order to avoid 'alert fatigue,' which could create indifference or doubt regarding the importance of the messages.

The agency was encouraged to consider public/private partnerships to design communication strategies and facilitate efforts to standardize anti-counterfeit communications and to augment and coordinate communication systems. The comments also said that costs to FDA and private partners should be kept to a minimum.

U. S. Department of Health and Human Services
Food and Drug Administration
Rockville, Maryland 20857