FDA Counterfeit Drug Task Force
Interim Report

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EXECUTIVE SUMMARY

FDA Commissioner Mark McClellan established the Counterfeit Drug Task Force in July 2003 as part of FDA's heightened battle against the growing threat of counterfeit drugs. Commissioner McClellan charged the Task Force with developing recommendations for achieving four fundamental goals: (1) preventing the introduction of counterfeit drugs, (2) facilitating the identification of counterfeit drugs, (3) minimizing the risk and exposure of consumers to counterfeit drugs, and (4) avoiding the addition of unnecessary costs on the prescription drug distribution system, or unnecessary restrictions on lower-cost sources of drugs.

The Task Force has reached several interim conclusions. First, there is no single "magic bullet" against the growing number of sophisticated counterfeiters; rather, a multi-pronged strategy to secure the drug supply could be much more difficult for counterfeiters to overcome than any single method. It could also be less costly, because a "one-size-fits-all" approach is unlikely to work for all parts of the complex prescription drug supply system. Second, although drug counterfeiters today are more sophisticated and better organized than ever before, there are many new technologies and approaches that have the potential to prevent and contain counterfeit drug threats. While most of these new approaches have not yet been fully developed, implemented, and tested, they hold the promise of a more secure drug distribution system in the years ahead. Third, because many of these promising ideas have not been fully developed, the Task Force believes that an opportunity for broad public comment is essential to guide its further work.

Consequently, the interim report contains a series of potential options that might be part of a multi-pronged approach to combat counterfeit drugs. The potential options are based on what the Task Force has learned to date from reports, other governmental agencies, and individual stakeholders (e.g., state governments, trade associations, consumer groups, drug manufacturers, wholesale distributors, pharmacies, consumers, academicians, manufacturers of anti-counterfeiting technologies).

The interim report also contains background information compiled by the Task Force on the U.S. drug distribution system and the vulnerabilities that facilitate the introduction of counterfeit drugs into the system.

The background sections also discuss how specific factors, such as emerging anti-counterfeiting technologies, industry business practices, public awareness, and the dissemination of information, affect the ability to deter and detect counterfeit drugs.

The discussion of the U.S. drug distribution system and these specific factors provide the context and basis for the potential options proposed for consideration by the Task Force. These options are in the areas of:

- Technology;
- Regulatory requirements and secure business practices;
- Rapid alert and response systems;
- Education and public awareness; and
- International issues.

Because a principal goal of this report is to stimulate public discussion of the most cost-effective way to keep the drugs used by Americans secure, these options are posed as potential options and are accompanied by a number of questions for the public, highlighting areas where the Task Force wishes to obtain further comment to inform its final report.

I. The Counterfeit Drug Task Force

A. Purpose of the Task Force

On July 16, 2003, Commissioner of Food and Drugs Mark McClellan, M.D., Ph.D., formed an internal FDA Counterfeit Drug Task Force to develop recommendations for steps FDA, other government agencies, and the private sector can take to minimize the risks to the public from counterfeit drugs and biologics (hereinafter, all references to "drugs" refers to both drugs and biologics) getting into the U.S. drug distribution system. This initiative is designed to enhance the existing safeguards that are in place to protect the nation's drug supply from counterfeit drugs.

Although FDA believes that domestic counterfeiting is not widespread, 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.

Counterfeit drugs pose significant public health and safety concerns. They may contain only inactive ingredients, incorrect ingredients, improper dosages, sub-potent or super-potent ingredients, or be contaminated. As a result, patients may be put at risk for serious adverse health consequences. For example, Procrit, a drug used by cancer and AIDS patients, was recently counterfeited and the drug was replaced with nonsterile tap water, which could have caused a severe infection of the bloodstream. In another recent counterfeiting incident, white tablets with "aspirin" imprinted on them replaced Zyprexa, a drug used for schizophrenia and acute bipolar disorder. This could have been particularly dangerous for patients who are aspirin-sensitive or aspirin-allergic or who have bleeding disorders. In addition, patients no longer received appropriate treatment for their illness. Counterfeiters also have been known to switch lower-strength drug for higher strength drug. As a result, patients receive lower than expected doses of drug, leading to ineffective treatment and therapeutic failure.

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. For example, in South-East Asian countries approximately 10% of drugs on the market are believed to be counterfeit. In China, authorities believe that for some drugs, counterfeits account for 50% of the product on the market. It is reported that in underdeveloped countries such as Argentina, Colombia, and Mexico, up to 40% of manufactured pharmaceuticals may be counterfeit.

B. Development of the Interim Report

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

As part of this effort, the Task Force has met with several government agencies, such as the Secret Service, U.S. Customs and Border Protection, the Bureau of Engraving and Printing, and the Department of Justice, as well as various individual private sector stakeholders. The Task Force has also reviewed reports prepared by, or on behalf of, federal and state governments, and heard from the public, including such stakeholders as pharmaceutical manufacturers, wholesale distributors, pharmacy associations, consumer groups, academicians, independent consultants, and manufacturers of anti-counterfeiting measures. As described in more detail below, the Task Force intends to continue these interactions before developing its final report.

Based on what it has heard to date, the Task Force believes that the most constructive approach to addressing the problem of counterfeit drugs lies in identifying vulnerabilities in the drug distribution system and addressing those vulnerabilities with a multi-pronged approach. So far, the Task Force has found considerable consensus about these vulnerabilities, as well as new opportunities to address them. The Task Force intends to build on these ideas to identify a set of broadly supported initiatives to improve the security of the U.S. drug supply.

C. What the Interim Report Contains

This interim report contains a series of ideas and potential options developed by the Task Force for consideration in each of the following areas: technology, regulatory requirements and secure business practices, alert systems, education and public awareness, and international issues. The potential options are in the form of potential actions that, if taken, may prevent the introduction of, and help to quickly identify, counterfeit drugs in the U.S. drug distribution system. These options do not represent the recommendations of the Task Force; rather, they are included in this report to stimulate further discussion and critiques, and to support the development of clear proposals that are likely to succeed. Many of the options discussed complement each other and are not mutually exclusive.

In its research and exploration of ways to address counterfeit drugs, the Task Force has been sensitive to the rising cost of drugs and that its efforts should not impose additional costs that could be borne by consumers nor impede access to less expensive, lawfully obtained drugs. In fact, this interim report includes potential options that may bring about cost savings to entities in the U.S. distribution system, which could reduce drug costs while at the same time reducing the likelihood that U.S. consumers would receive a counterfeit product.

Additionally, Section IV of this interim report contains a series of questions highlighting areas where the Task Force wishes to obtain further information to help inform its final report.

D. Development of the Final Report

The Task Force plans to continue gathering information from individual stakeholders and members of the public as it prepares its final report which is scheduled for release in January 2004. As part of this effort, the Task Force will hold a public meeting and technology forum on October 15, 2003, during which the Task Force will hear testimony from the public on the problem of counterfeit drugs and will learn more about specific anti-counterfeiting technologies. See the counterfeit drug initiative web page at www.fda.gov for more information and a copy of the notice announcing the meeting. The questions in this report supplement the questions published in the notice.

The Task Force recognizes that the options presented in this report are based on what it has heard and reviewed to date, and looks forward to receiving comments and information that will provide further basis for the final report and recommendations of the Task Force.

E. Goals of the Initiative

In the final report, the Task Force plans to issue recommendations that will ensure that the U.S. drug distribution system continues to be the safest, most secure system in the world. Features of the system might include:

- the use of cost-effective technologies, including many new and emerging technologies, to authenticate and track drugs from the point of manufacture to the point of dispensing to deter and detect the introduction of counterfeit drugs;

- exercise of a high level of diligence by all purchasers to ensure that drug products are authentic, in accordance with industry standards and secure business practices;

- a regulatory scheme that minimizes the burdens placed on each participant in the system; and

- well-informed stakeholders and consumers.

II. Background: Vulnerabilities in the U.S. Drug Distribution System

In order to better understand how counterfeit drugs are introduced into the U.S. marketplace, the Task Force examined the drug distribution system in the U.S. to better understand existing vulnerabilities.[1]

A. The Drug Distribution System

Congress created a framework of laws intended to maintain high public confidence in the U.S. drug distribution system and the safety and efficacy of drug products. States also have enacted laws and regulations that are intended to complement Federal oversight to further protect the integrity of the U.S. drug distribution system. Together, State and Federal legislation and regulations work to provide security in the nations drug supply.

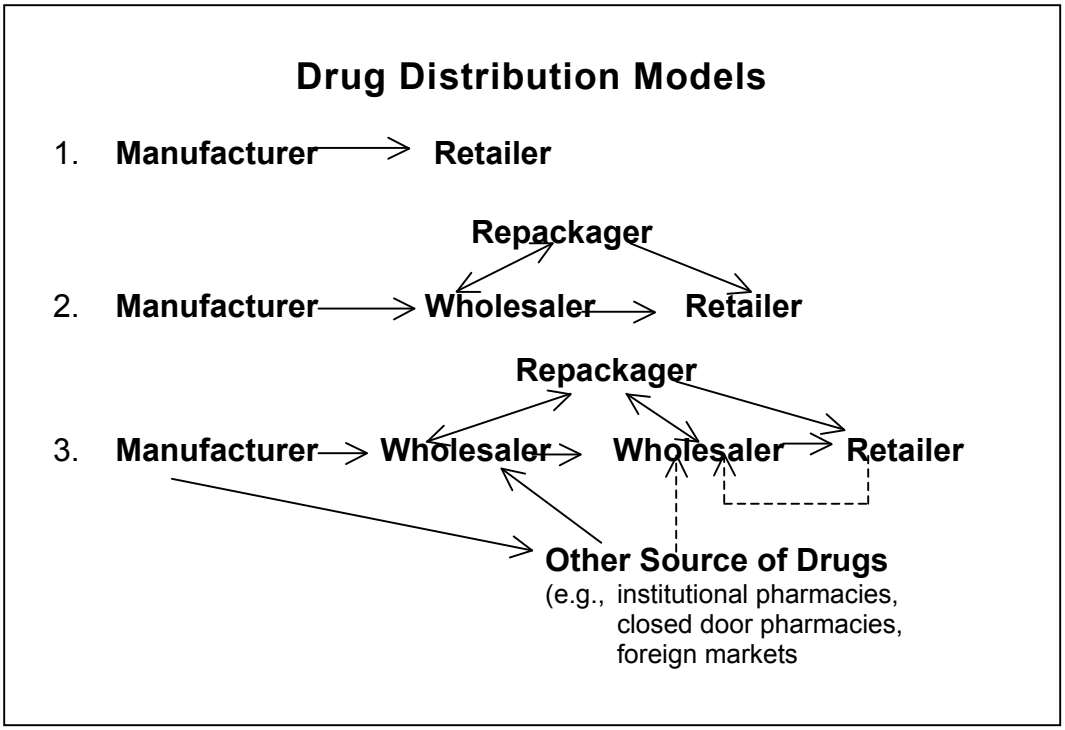
The Task Force reviewed and considered information from published reports, criminal investigations, and other sources describing the drug distribution system. What follows is a brief summary of what the Task Force has learned to date.

There are three large wholesalers who account for about 90% of the primary wholesale market. In addition, there are many smaller wholesalers who may have full or partial product lines and who may or may not sell nationally or regionally. Some of these wholesalers concentrate in the "secondary" wholesale market, i.e., they purchase selected drug products from wholesalers and they resell to other wholesalers, including large wholesalers, as well as pharmacies. They generally purchase discounted drug products. There are many reasons why sales from one wholesaler to another may benefit consumers. These may include: 1) taking advantage of price discounts available on certain legitimate drug products, (e.g., when a manufacturer or wholesaler has a temporary overstock or purchases excessive product on speculation that the manufacturer will raise prices), 2) low volume transactions (e.g., involving drugs that are used only occasionally in special populations), 3) quick turnaround (e.g., permitting a wholesaler or pharmacy to meet a temporary and unexpected increase in demand

[1] The Food Drug and Cosmetic Act (the Act) defines a counterfeit drug as "a drug which, or the container or labeling of which, without authorization, bears the trademark, trade name, or other identifying mark, imprint, or device, or any likeness thereof, of a drug manufacturer, processor, packer, or distributor other than the person or persons who in fact manufactured, processed, packed, or distributed such drug and which thereby falsely purports or is represented to be the product of, or to have been packed or distributed by, such other drug manufacturer, processor, packer, or distributor." (21 U.S.C. 201(g)(2))

for a drug), or 4) sale to a remote area (e.g., sales to a small rural community). Figure 1 depicts drug distribution models in the U.S.

Figure 1



[Figure 1 depicts three models showing the movement of drugs through the U.S. drug distribution system. (The dotted lines indicate potential illegal sales.) In the simplest situation, the manufacturer sells directly to a retailer. However, in many instances, there can be one or more wholesalers, or even a repackager, who handles the drug before it reaches the retailer. It is in these intermediate steps, particularly when the wholesaler(s) and/or repackager(s) obtain products from sources other than the original manufacturer, that the greatest opportunities for compromising the security of the U.S. distribution system exist.]

B. Sources of Counterfeit Drugs

For a variety of reasons, counterfeit drugs currently are most likely to be introduced as part of a drug distribution process involving multiple wholesalers. However, it is important to recognize that criminal activity to introduce

counterfeit drugs can occur at any stage in the drug distribution system, so that safeguards are needed in all of the transaction processes.

Many drugs in the distribution system are also "repackaged". In the U.S., wholesale drugs in bulk containers are often repackaged into smaller containers prior to sale to an end user. Repackaging operations are performed by independent entities, wholesale distributors, or by distribution centers owned by large pharmacies. In the current distribution system products are repackaged for several legitimate reasons, such as to improve efficiencies for automated systems. In Europe, products are packaged in quantities that relate to a course of treatment (unit of use,) in general, obviating the need for repackaging.

The Task Force heard from law enforcement personnel that when counterfeit drugs are identified, they are often associated with diversion of the drugs that they purport to be. Diversion is the sale of drugs outside of the distribution channels for which they were originally intended. Diverted drugs can originate domestically, when there is illegal redirection of prescription drugs from other legitimate sources, such as free samples supplied to health care providers or lower-priced drugs intended for nonprofit clinics or Medicaid programs. Additionally, diverted drugs can originate in a foreign market, when donated or lower-priced product intended for use in one country is diverted to another country where the market price is higher. Counterfeit drugs generally are associated with the practice of diversion. Our current regulatory system does not have legitimate, regulated channels for such diverted drugs (even if authentic) to re-enter the drug distribution system. Consequently, there is no reliable mechanism in place to distinguish effective authentic lower-cost drugs from drugs that simply appear to be so, but are not legitimate and may be harmful.

Diversion facilitates the entry of counterfeit drugs into the U.S. distribution system because those individuals or entities that sell or purchase diverted drugs are less able to verify the integrity of these drugs, because they are purchased outside the normal distribution chain and without the usual regulatory safeguards. As a result, counterfeit, substandard, or otherwise adulterated or misbranded products may become commingled with authentic drugs in the U.S. distribution system. Because counterfeiting is often associated with drug diversion, steps to secure the drug supply against counterfeits may also make criminal drug diversion more difficult.

C. Points of Vulnerability in the U.S. Drug Distribution System

As noted above, some business practices that may serve certain desirable purposes, such as discounted pricing, can create opportunities for criminals to introduce counterfeit drugs into the drug distribution system. These practices represent potential vulnerabilities in the drug distribution system and require a high level of diligence by participants in the drug distribution chain in order to deter and detect counterfeit drugs. A more secure distribution system should

include additional features to prevent counterfeit entry beyond the practice of due diligence by all participants.

For reasons that often benefit consumers, a manufacturer may sell a drug product at lower prices to certain end users or wholesalers. When this happens, the cost differential between the discounted price and the market price (which is based on the manufacturer's usual list price and paid by other end users) can foster multiple profitable transactions before sale to an end user. Both wholesalers and end users who purchase drug products at discounted prices can initiate this chain of transactions. A drug product undergoing multiple transactions between the time it is sold by the manufacturer and the time it is bought by an end user, should be properly authenticated (e.g., via inspection, examination of the product's pedigree, or use of track and trace technology) by each purchaser in order to minimize the possibility that a counterfeit product has been substituted by an unscrupulous entity during one of the transactions.

Therefore, lack of a high level of diligence by members of the U.S. drug distribution chain can facilitate the introduction of counterfeit drugs into the drug U.S. drug supply. Investigations performed by Federal and State authorities have repeatedly shown the existence of illicit nationwide networks designed to capitalize on the inadequate due diligence performed by members of the drug distribution system in order to introduce potentially unsafe diverted and counterfeit drugs into the U.S. drug distribution system.

As drug prices continue to rise, opportunities to obtain lower cost drugs become increasingly important. However, because potential cost savings from discounted pricing provides a target for counterfeiters, the need for due diligence in this circumstance, particularly when multiple transactions occur, also increases.

However, even with a heightened level of vigilance by parties participating in single or multiple transactions or by those seeking lower-cost versions of drugs, there are weaknesses in the drug distribution system that can facilitate the entry of counterfeit drugs. Below, we discuss in more detail, several points of vulnerability in the U.S. distribution system that the Task Force identified.

- *Incomplete Pedigrees*—A pedigree is a statement of origin that traces the drug from the point of manufacture and contains information about all transactions that the product undergoes until it reaches the end user. Products that have incomplete pedigrees, such as pedigrees that do not include all the transactions involving a drug from the time it leaves the manufacturer to the time it is sold to a consumer, make it more difficult to track and trace the authenticity of those drug products than products that have more complete pedigree information.

- *Inadequate or No Authentication*—It is important for purchasers in the U.S. drug distribution chain to ensure that the product they are purchasing is the genuine article (i.e., authenticate the product). Tools and processes are readily available to copy drug products and their

labeling and packaging to such an exact degree that even the manufacturer of the authentic product cannot tell if it is real or fake. On the other hand, technologies are also available (or will be in the near future) to identify whether the product that they are purchasing is authentic or counterfeit. Unfortunately, these authenticating technologies often are not incorporated into the drug product, labeling, or packaging.

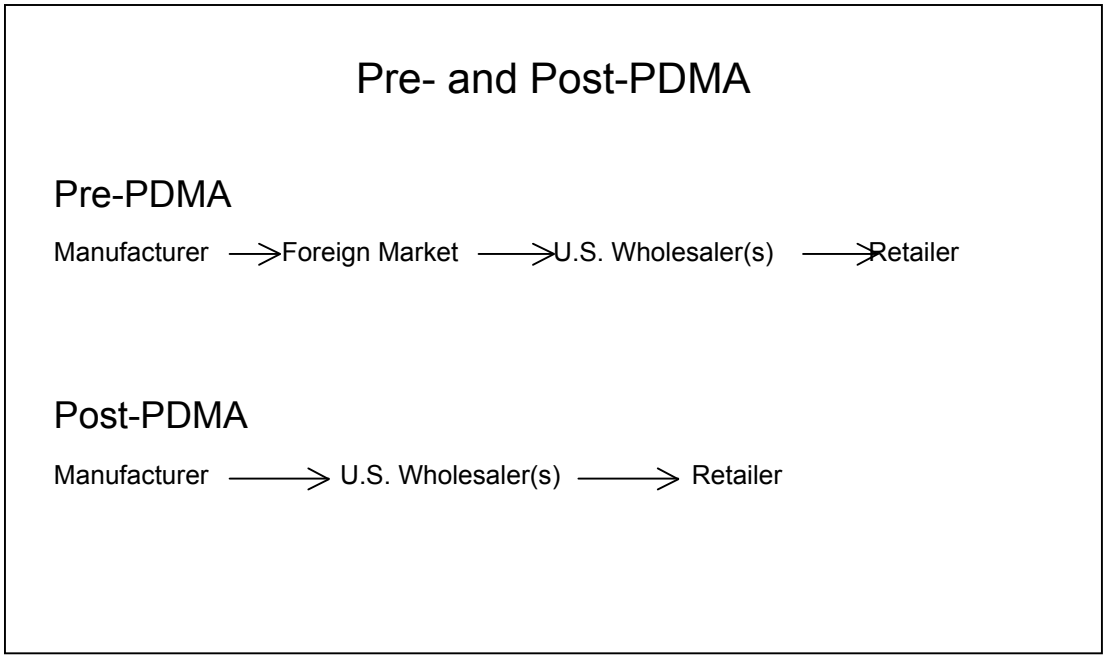
- *Importation*—Prior to the passage of the Prescription Drug Marketing Act (PDMA), including section 801(d)(1), drugs manufactured in the U.S. could go to a foreign market and then be reimported into the U.S. This became a common entry point for the introduction of adulterated and counterfeit drugs into the U.S. drug distribution system. Such products posed a public health problem because they were found to be subpotent, lacked active ingredients, contained ingredients that could pose a severe health hazard if taken by a susceptible person (e. g., aspirin), lacked adequate labeling, or were not approved drug products. For example, pre-PDMA, in 1985, over 2 million counterfeit tablets of Ovulen-21 from Panama were widely distributed throughout the U.S. Similarly, in 1985, a counterfeit version of Ceclor, an antibiotic widely used at that time, found its way into the U.S. drug distribution from a foreign source.

  In response to this public health problem, Congress passed PDMA, which prohibits reimportation of drugs by any entity other than the manufacturer. Figure 2 depicts the path of a drug in the U.S. distribution system, both before and after passage of the PDMA. The FDA and the States do not have oversight or authority over the foreign marketplace. Under current law, the FDA only has authority over foreign manufacturers when they submit to FDA oversight as part of a new drug application. (See 21 USC 355.) In addition, under current law, FDA has no authority to inspect or assess the practices used in foreign drug distribution systems. Obtaining drugs from a foreign distribution system further exacerbates existing vulnerabilities, similar to, but more severe than, those that facilitate domestic diversion. (See Figure 1, Model 3.) However, unlike entities engaged in domestic diversion, foreign counterfeiters remain outside the reach of U.S. law enforcement. Congress prohibited reimportation to protect American consumers from receiving counterfeit, substandard, or otherwise adulterated drugs.

  Furthermore, when consumers order medications from outside the U.S. (e.g., internet purchases, cross-border purchases), whether safe or unsafe, a portal of entry is created for counterfeit drugs into the U.S. distribution system. Counterfeiters can take advantage of this entryway by combining many small purchases from foreign countries into one and selling them to U.S. wholesalers or other unsuspecting entities. Due to the extensive resources involved in preventing small quantities of drugs from entering the U.S., as the volume of unapproved drug

imports increases, it is more difficult for FDA to use its existing resources to identify and stop unsafe importations.

Figure 2



- *Repackaging*—Repackaging may destroy anti-counterfeiting measures used in the original packaging and labeling of the drug. It may also provide a point of entry for expired, adulterated, or counterfeit drugs into the distribution system because they may be repackaged in a way that makes them appear to be legitimate products. Lastly, counterfeit and diverted product may be commingled with authentic product during the repackaging process and find its way to an end user.

- *Tamper-Evident Packaging*—Currently, many prescription drug products do not utilize tamper-evident features. Without tamper-evident features, the original packaging may be reused for counterfeit or diverted product and thereby be more easily passed off as legitimate product. The reuse of old prescription drug containers found in trash facilities or taken from hospitals and clinics is also a significant problem because no tamper-evident feature has to be replicated, thereby enabling easy reuse of the packaging to distribute counterfeit, adulterated, or unapproved drugs. While tamper-evident packaging is important, it is also worth noting that counterfeit drugs can be repackaged into legitimate-appearing packaging (including features intended to mimic legitimate tamper-evident features), so that packaging alone cannot assure that drugs have not been counterfeited.

D. Background: Regulatory and Legislative History

1. Prescription Drug Marketing Act

As previously alluded to, Congress addressed some of these vulnerabilities by enacting the PDMA in 1988, which was amended in 1992 by the Prescription Drug Amendments. Among other things, the PDMA:

- requires State licensure of wholesale distributors of human prescription drugs;

- requires wholesale distributors of human prescription drugs in interstate commerce to provide a statement of origin, also known as a drug "pedigree", which traces each prior sale, trade, or purchase of the prescription drug, to and from each wholesale customer prior and subsequent to the sale of the drug to that wholesaler, but exempts manufacturers' "authorized distributors;"

- with certain exceptions, prohibits the resale of prescription drugs that have been purchased by a hospital or other health care entity or that have been donated or supplied at a reduced price to a charitable organization.

In 1999, FDA published final regulations implementing the provisions of the PDMA. The provisions concerning the pedigree requirements at 21 CFR 203.3(u) and 203.50 were stayed by FDA because of valid concerns expressed by industry, trade associations, and Congress about implementing these provisions. Such concerns included the high cost and logistics of maintaining a pedigree and occasional inability to obtain a transaction history from the prior distributors and the manufacturer, thus calling into question the usefulness of the pedigree. Taking steps to address these requirements using traditional methods could impose substantial costs, at a time when access to affordable drugs is also a major policy concern.

In 2000, FDA held a public hearing to discuss these concerns. In 2001, FDA submitted a Report to Congress outlining the concerns raised by the secondary wholesale industry. The agency noted that in order to enable secondary wholesalers to fully comply with the pedigree requirements, Congress would have to amend section 503(e) of the Act to enable them to get the transaction history from all prior purchasers of the drug (because, currently, wholesalers who are authorized distributors of record are exempt from providing this information.)

In order to give Congress time to consider the information and conclusions contained in the agency's Report to Congress and to determine if legislative

action was appropriate, FDA subsequently instituted an additional stay of the provisions until April 1, 2004.

In addition to being costly, tracing a drug pedigree on paper, as envisioned in the PDMA, is subject to multiple record keeping failures, and may be subject to fraud. As discussed below, there are many promising developments in anti-counterfeiting technology that will enable the creation of an electronic pedigree for a drug product, thus reducing the need for paper pedigrees. Other steps discussed below can also help address the weaknesses identified in the PDMA. These new approaches are consistent with the desired movement toward electronic health information systems to prevent errors and adverse events, and would also make it easier to maintain the high level of diligence needed throughout the drug distribution system to prevent the introduction of counterfeit drugs.

2. Model Practice Act

As part of the implementation of PDMA, in 1990, FDA published a final rule containing "Guidelines for the State Licensing of Wholesale Prescription Drug Distributors." The guidelines were codified at 21 CFR Part 205. The guidelines include the minimum standards, terms, and conditions for the storage and handling of prescription drugs and for the establishment and maintenance of records of their distribution. The guidelines followed, among other things, the "Model Regulations for Wholesale Drug Distribution" (Model Rules) issued by the National Association of the Boards of Pharmacy (NABP), which were previously issued as an example for States to adopt in order to comply with the PDMA. Subsequently, all 50 states have enacted some sort of legislation to implement the PDMA.

As the introduction of counterfeit drugs has increased over the past several years, some states, such as Florida and Nevada, have adopted laws and regulations with more stringent requirements intended to minimize the risk of counterfeit drugs appearing in their state. The Task Force believes that such steps could have an impact on the nationwide problem of counterfeit drugs.

To this end, the Task Force is working closely with the NABP to update the Model Rules and is in the process of reviewing the 50 state practice acts that govern wholesale distribution of prescription drugs, identifying strengths and weaknesses of those acts, and suggesting where the Model Rules can be updated. Based on its findings to date, the Task Force views the following as important areas for States to focus on in updating their Model Rules: requirements for licensure, qualifications of employees, handling and storage of drugs, site security, inspection and examination of drugs, record keeping, availability of records to inspectors and law enforcement personnel, due diligence, administrative subpoena power, and criminal penalties.

3. Penalties and Enforcement

The Task Force has reviewed the current applicable criminal statutes and sentencing guidelines for various types of counterfeiting and has found that the penalties for counterfeiting drugs are substantially less than for other types of counterfeiting, such as counterfeiting registered trademarks. 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. Also, the U.S. Sentencing Commission guidelines currently include FD&C Act felonies at the lowest level of all federal crimes. Yet, counterfeiting of drugs may create substantial risks to the health and safety of a large number of consumers.

The Task Force has reviewed the statutes under which drug counterfeiting charges may be brought, as well as provisions that may streamline investigations and facilitate the seizure of counterfeit drugs and the forfeiture of illegal proceeds. The Task Force heard from some organizations that, as implemented to date, these penalties may not be severe enough to deter and punish those responsible for counterfeiting drugs.

The Task Force also reviewed the subpoena authority currently available to certain regulatory agencies, such as the Internal Revenue Service and the Bureau of Customs. The subpoena authority of those agencies is related to their statutory roles and responsibilities, and in conjunction with their other authorities, supports the efficient execution of their mission when other approaches (e.g., surveillance and tracking systems) are unable to provide the information required to address public threats.

E. Background: Technology Issues

1. Types of Anti-Counterfeiting Technologies

Two types of anti-counterfeiting technologies have existed for many years:

- Authentication technologies, and
- Track and Trace technologies.

Authentication technologies fall into three groups:

- **Overt** technologies are protective measures that are easily visible to the eye, such as holograms, color shifting inks, and some watermarks.
- **Covert** technologies are protective measures that are not visible to the eye and frequently require special equipment for visualization (and

authentication). These include some watermarks, certain inks and dyes that fluoresce or absorb ultraviolet light, and invisible bar codes.

- **Forensic technologies** are protective measures that require sophisticated analytical equipment, usually found in a forensic chemistry lab, in order to be identified. These include chemical markers, taggants, and other unique chemical properties of a substance.

Track and trace technologies include:

- **Radio-frequency identification (RFID)** is a technology that involves the placement of electromagnetic chips/tags that contain product specific information onto cartons, pallets, and individual products. The system includes the tags, antennae affixed to the tags, readers to receive the data in the tags, and an information database that is used to authenticate and track the product as it moves through the distribution system.

- **Barcodes** are symbols (representing an alpha numeric value) printed on labels that are read by a scanner and used to identify drug products. Bar codes can be combined with covert elements (e.g., security ink) that also allow them to function as authentication technologies.

Appendix A to this report contains a list of some basic types of authentication and track/trace technologies along with some of their capabilities and limitations.

2. Utilization of Anti-Counterfeiting Technologies

The Task Force recognizes that the functions of authentication and track/trace technologies are complementary. In order to reduce the likelihood of counterfeit drugs being introduced, and to increase the likelihood of identifying counterfeit drugs in the U.S. drug distribution system, both technologies should be utilized. The information reviewed by the FDA to date demonstrates that no single authentication or track/trace technology is a complete solution to facilitating the identification, and preventing the introduction, of counterfeit drugs into the marketplace. Law enforcement officials and other government agencies shared with FDA their experiences with counterfeiting of currency, credit cards, checks, and other documents. Their universal advice is that multiple technologies and measures must be utilized because determined counterfeiters are able to defeat many anti-counterfeiting measures within 18-24 months after the measure is implemented. Therefore, multiple strategies and a continuous evolution of technology are necessary to thwart criminal activity.

The Task Force has heard that track/trace technologies should be incorporated at the point of manufacture, used throughout the distribution system, and inactivated/destroyed at the time of dispensing. When track/trace technologies are used at a pallet and case level, they have the capability of following the

product at each point in the distribution chain. To be maximally effective for authentication purposes, track/trace technologies should be incorporated at the product (individual package) level in addition to the case and pallet level so that individual product, rather than only bulk shipments, can be followed.

The Task Force has learned that the use of radio frequency identification (RFID) chips is undergoing pilot testing in several venues; however, widespread use of RFID may not occur for several years. Aside from the need to work out technical problems, (e.g., attaining 100% read rates,) a significant reason for this delay is that RFID and some other sophisticated technologies will not work without a system-wide infrastructure and an integrated database. An integrated database is one that is accessible to all users in the distribution chain for viewing data and contributing to the tracking of a particular product. Such databases and the associated "reading" technologies could take several years to develop and gain widespread adoption throughout the marketplace. Issues that need to be resolved include: Who will create the database? Who will own the data? And, who has access to the data?

If all entities in the drug distribution chain use RFID chips or other electronic track/trace technology, an "electronic pedigree" will be created de facto for the product. An advantage of an "electronic pedigree" is that it is harder to forge than a paper pedigree. However, for an electronic pedigree to become universally adopted, industry or national standards would have to be developed and implemented.

The Task Force has learned that the use of authentication technologies varies by pharmaceutical company and product. In general, authentication technologies are more widely used than track/trace technologies. However, the way they are used and the number that are used vary. For example, the Task Force has learned that combinations or layers of authentication technologies are more likely to be used in products at high risk for being counterfeited. On the other hand, products considered to be at lower risk may have fewer anti-counterfeiting measures incorporated into their manufacturing, packaging, or labeling.

Moreover, in the event that a suspect counterfeit product is found, there is a need for FDA and stakeholders to rapidly identify whether the labeling, packaging, and product are authentic. Currently, there is no database for FDA, other government regulatory agencies, or stakeholders to use which contains up-to-date information about authentic products, packaging, labeling, and utilization of anti-counterfeiting measures. Such a database could expedite confirmation of a suspect counterfeit drug product's authenticity.

3. Cost/Benefit of Anti-Counterfeiting Technologies

The Task Force has heard a great deal about the costs of adopting anti-counterfeiting technologies. These include costs associated with:

- Purchase of the technology;

- Purchase of associated equipment (e.g., barcode scanners, RFID receivers, access to electronic databases) and services;
- Integrating the technology into the manufacturing process;
- FDA review, if required, for the technology;
- Adopting new anti-counterfeiting measures as old ones are defeated;
- Creation of infrastructure throughout the distribution system.

To date, the Task Force has heard less about the potential benefits of adoption of anti-counterfeiting technologies beyond greater assurance of drug safety. In addition to the public health and economic benefits associated with a reduction in the number of counterfeit drugs, other benefits may include:

- Improved inventory management and control (with resulting reductions in inventory expenses for distributors and pharmacies);
- Reduced labor cost due to automation;
- Reduction in theft and product loss due to other causes;
- Reduction in the amount of diverted product;
- Improved ability to recall product;
- Protection of drugs from intentional tampering;
- Protection of drugs from being used in an act of terrorism.

An area of focus for the Task Force as it gathers more information on anti-counterfeiting technologies will be to find ways to maximize the benefits of new anti-counterfeiting measures while minimizing their costs.

F. Background: Health Professional and Industry Issues

1. Secure Business Practices

Given the complicated nature of many features of the drug distribution system, the business practices of the entities involved in those transactions (e.g., wholesalers, repackagers) plays a critical role in determining the ability and likelihood of introducing counterfeit drugs into the supply chain. These business practices may also play a role in the ability of stakeholders to identify counterfeits before they reach a consumer.

Industry practices in such areas as recordkeeping, inspection and examination of drugs, facility and information security, package disposal, performance of 'due diligence' on business partners, and establishing criteria for determining with whom they do business are all crucially important for the integrity of the drug distribution system.

Based on its research to date, the Task Force is not aware of any pertinent benchmarks or industry standards for business practices among pharmaceutical manufacturers, wholesalers, repackagers, and pharmacies with regard to the sale and purchase of drugs. The lack of adequate benchmarked industry standards is important because legitimate businesses are often involved in the purchase and sale of counterfeit drugs and therefore can be involved, unknowingly, in allowing counterfeit drugs to reach consumers. In addition, the lack of such standards creates opportunities for criminals to introduce unsafe drugs into the U.S. drug distribution system.

The Healthcare Distribution Management Association (HDMA) has submitted a draft document entitled "Recommended Guidelines for Pharmaceutical Distribution System Integrity," which was endorsed by the Pharmaceutical Distributors Association (PDA), for the Task Force to consider in its deliberations. The document is a set of draft voluntary guidelines for pharmaceutical wholesalers to use for screening another pharmaceutical wholesaler prior to establishing a business relationship. It emphasizes the need to perform "due diligence" by requesting certain information, performing background checks, and inspecting the facilities of the potential business partner.

The Task Force will continue to work with HDMA, PDA, and others to gather information about current and best practices in the pharmaceutical industry prior to considering any final recommendations about the nature and extent of any changes to current industry practice that might reduce the risk of counterfeit drugs entering the distribution chain

2. Rapid Alert and Response Systems

Identifying suspect counterfeit drugs in the distribution system is important to prevent sale of the counterfeit product to the patient. While consumers can help, wholesalers, distributors, repackagers, and pharmacists are often best situated to identify and report suspect counterfeit drugs. Recognizing this important role, the Task Force believes that steps should be taken to facilitate reporting of suspect counterfeit drugs and that a central FDA voluntary reporting mechanism be used for reporting by the public.

Recently, a variety of industry groups have begun to take voluntary steps to address this problem. For example, earlier this year, the pharmaceutical industry announced a voluntary program, whereby Pharmaceutical Research and Manufacturers of America (PhRMA) member companies agree to notify FDA's Office of Criminal Investigations (OCI) within five working days of determining that there is a reasonable basis to believe that a product has been counterfeited. OCI has received several reports since that April 2003. OCI is currently working with industry to standardize reporting requirements and otherwise improve communications. The program also applies to counterfeits discovered in foreign countries if there is clear evidence that the counterfeits are intended for distribution in the United States. HDMA recently announced similar steps that their member companies will take in notifying FDA of suspect counterfeit drugs.

Currently, health care professionals and consumers use FDA's MedWatch system for reporting adverse events associated with medical products as well as product problems. Policies and procedures are in place to ensure that the information is conveyed to appropriate agency personnel for follow up. For example, if there is a problem with a product (e.g., broken tablets, lack of efficacy) the information is analyzed and/or investigated to determine whether there are steps manufacturers may need to take to correct the problem. Additionally, over 150 health care professional, consumer, and trade organizations have partnered with MedWatch to help disseminate information and alerts generated by MedWatch. The Task Force believes that this system can be adapted to receive reports of suspect counterfeit drugs and communicate important information in the event a counterfeit drug is identified.

As described below, the Task Force is exploring the creation of a counterfeit drug alert network, which would draw on all of these elements and could be utilized to disseminate information when a counterfeit drug is identified. Such a network also could be used as a vehicle for educational messages.

G. Background: Education and Public Awareness Issues

The Task Force believes that an educated, vigilant public is an invaluable defense against counterfeit drugs filtering into the U.S. pharmaceutical market. Consumers and health professionals need to know how to proactively avoid these counterfeits. They also need to be familiar with what to look for when faced with a potential counterfeit and the steps that need to be taken if they are suspicious that they have encountered one.

The Task Force explored what appropriate role FDA and its partners could play to educate potentially affected groups. A logical first step to take would be to identify specific stakeholders that would most likely be affected by counterfeit drugs. The next step would be to craft appropriate messages and identify effective communication tools to accurately reach these diverse stakeholders. This step is very important because various communities and professional groups receive health information in different ways.

The Task Force recognizes that once a counterfeit is identified in the stream of commerce, public officials must quickly act to remove the counterfeit drug from the marketplace. However, at the same time, while getting this information out to the public, officials need to take care not to alarm unaffected consumers, thereby causing them to discontinue necessary therapy. The FDA has long held the position that protection of the public health will remain its number one mission, even if public notifications of a counterfeiting scheme might hinder the criminal investigation to determine who is responsible for the counterfeiting.

As part of its assessment of current communication channels, the Task Force consulted with numerous agency components that oversee communication channels potentially pertinent to anti-counterfeit communications. Information from consumer groups, health care provider associations, media representatives, trade organizations, and representatives of state governments/enforcement groups was also reviewed to better understand the current information flow processes between the FDA and outside stakeholders.

Based on this information, the Task Force made the following preliminary assessment:

- There is a need for more comprehensive efforts to educate the public about the threat of counterfeit drugs, how to identify them, and how to minimize the risk of receiving counterfeit drugs. Figure 3 is an example of the type of educational messages that may be used in an educational campaign.

- Efforts to educate pharmacists and other health professionals about current counterfeit events and how to handle these situations exist, but could be improved.

- When a counterfeiting event occurs, there are sometimes delays of varying degrees in alerting and updating the appropriate health professional about the problem. When the messages are delivered, they may not be adequately tailored to the various audiences to be helpful to them. Also, stakeholders complain they have to work too hard to access timely, accurate information - a proactive alarm system was named as a potential solution

- There may be additional opportunities to work with health care providers and manufacturers to capture data that may help identify counterfeits.

What Can Consumers Do to Protect Themselves from Counterfeit Drugs?

1. **To avoid purchasing "buyer beware" drugs, it's safest to purchase ONLY from U.S. state-licensed pharmacies, where the FDA and state governments can assure the safety of drug manufacturing, packaging, distribution, and labeling.**

2. **If purchasing over the internet, make sure the website has the Verified Internet Pharmacy Practice Sites Seal (VIPPS).**

3. **Be vigilant about your medicine. Check for changes in packaging, labeling, color, taste, or shape of a pill. Look out for unanticipated side effects.**

4. **If you suspect you have a counterfeit drug:**

    a. **Contact the pharmacist that dispensed the drug; OR**

    b. **Call 1-800-FDA-1088; OR**

    c. **Contact your doctor.**

III. Potential Options for Improving Prescription Drug Security

Based on what it has heard and reviewed to date, the FDA Task Force on Counterfeit Drugs is listing a series of preliminary options 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.

The potential options are premised on several interim conclusions reached by the Task Force. First, there is no single "magic bullet" against the growing number of sophisticated counterfeiters; rather, a multi-pronged strategy to secure the drug supply could be much more difficult for counterfeiters to overcome than any single method. It could also be less costly, because a “one-size-fits-all" approach is unlikely to work for all parts of the complex prescription drug supply system. Second, although drug counterfeiters today are more sophisticated and better organized than ever before, there are many new technologies and approaches that have the potential to prevent and contain counterfeit drug threats. While most of these new approaches have not yet been fully developed, implemented, and tested, they hold the promise of a more secure drug distribution system in the years ahead. Third, because many of these promising ideas have not been fully developed, the Task Force believes that an opportunity for broad public comment is essential to guide its further work.

The Task Force notes that these options are not mutually exclusive. In general, these options could be implemented together or independent of each other.

A. Technology

The Task Force heard from many groups and individuals. According to what we have heard, appropriate long term goals for the use of technology include achieving an electronic pedigree and incorporation of authentication measures for all drug products. However, due to the emerging nature of many of these technologies, a phased in approach for their implementation should be considered. With this in mind, the adoption of one or more of the following options concerning the use of technology to deter and detect counterfeit drugs,

by the Federal government or the private sector, as appropriate, might reduce the likelihood of counterfeit drugs from entering the U.S. drug distribution system and/or reaching a U.S. consumer:

1. 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, as is now done in many nations;

2. Use tamper evident packaging from the point of manufacture, with labeling that notes the tamper evident feature, for all dosage forms, active pharmaceutical ingredients (APIs), and bulk chemicals;

3. Incorporate for all drug products at least two types of validated anti-counterfeiting technologies into packaging and labeling at the point of manufacture with at least one of these technologies being covert (i.e., not made public, and requiring special equipment or knowledge for detection) using a phased in approach starting with those products at high risk of being counterfeited and where the introduction of counterfeit product poses a serious health risk;

4. Incorporate for all drug products a taggant, chemical marker, or other unique characteristic(s) into the manufacturing process that is only identifiable with the use of sophisticated analytic technologies using a phased in approach starting with those products at high risk of being counterfeited and where the introduction of counterfeit product poses a serious health risk;

5. Create an electronic database of drugs and biologics for authentication purposes, which consists of photographs of the product, packaging and labeling information, and the anti-counterfeiting measures utilized in the packaging, labeling, and product itself;

6. Achieve the goal of the pedigree requirements by phasing in track and trace technology (i.e., electronic pedigree) for all drugs and biologics starting at a case and pallet level for products at "high risk of being counterfeited" and progressively including all products at the case, pallet, and package level. The technology should have an integrated infrastructure that is able to track and trace products at all points in the distribution chain from manufacturer to end user;

7. On an interim basis, because the technologies described above may take several years to implement, all drugs and biologics "at high risk of being counterfeited", should be tracked and traced either (1) By limiting the number of transactions of the product (e.g., shipping the product from the manufacturer either (a) directly to the retailer or health care entity, (b) to the retailer or health care entity through a single licensed wholesaler who would sell the product directly to retailers or health care entities, (c) identifying steps that multiple wholesalers can implement to reduce the risk of counterfeit

introductions), or (2) By using available track and trace technology, identifying the drug at least at the case and pallet level, and preferably at the product level, throughout the distribution system;

8. Issuance of an FDA guidance document concerning the appropriate use of anti-counterfeiting technologies as well as the FDA application and review process for incorporating or changing taggants, chemical markers, or other unique characteristic(s) of the product;

9. Issuance of an FDA guidance document concerning physical site security and supply chain integrity.

B. Secure Business Practices and Regulatory Requirements

The Task Force heard that the state requirements for licensure of wholesale distributors need to be updated and that the standards for certain business practices among the entities involved in the U.S. drug distribution system are insufficient. The following options, based on what we have heard, relate to secure business practices that affect the ability to deter and detect counterfeit drugs:

10. Continue to work with NABP to update their Model Rules for Licensure of Wholesale Distributors, using the Florida statute as a model where appropriate, in the following areas: requirements for licensure, qualifications of employees (especially those who handle drugs), storage and handling of drugs, site security (both for facilities and information), inspection and examination of drugs, record keeping, availability of records to inspectors and law enforcement personnel, due diligence with respect to business partners and contractors, administrative subpoena power, and criminal penalties; update FDA regulations under 21 CFR 205, as appropriate, to make it consistent with updates to the NABP Model Rules for Licensure of Wholesale Distributors;

11. Develop sets of "secure business practices" which would be voluntarily adopted by manufacturers, wholesalers, repackagers, and pharmacies. Best practices would be identified in areas such as: employee qualifications, security of physical facilities and information systems, package disposal, dealings with business partners and contractors, inspection and examination of products, record keeping, etc.;

12. Designate, by entities such as manufacturers, wholesalers, re-packagers, and pharmacies, an individual or team to coordinate security and anti-counterfeiting activities. Such activities would include quality improvement, monitoring and use of anti-counterfeiting technologies,

and regular review of the entities security and anti-counterfeiting measures;

13. Timely sharing with FDA, by manufacturers, of relevant market tracking and trending data and the analysis of these data for use as a means of identifying counterfeit or diverted product in the marketplace.

C. Rapid Alert and Response Systems

The Task Force heard that there is a need to strengthen the systems used for reporting by, and alerting of, stakeholders and the public as to the existence of counterfeit drugs. The following options, based on what we have heard, relate to alerts systems for counterfeit drugs.

14. Enhance the MedWatch Alert System for use as a tool to receive and disseminate timely information about counterfeit drug products, especially identification of suspect drug product;

15. Create a counterfeit alert network through use of existing, or newly developed, communication tools that allow reception, dissemination, and sharing of information about counterfeit drugs in a timely manner (e.g., to pharmacists, manufacturers, wholesalers, and law enforcement and public health officials);

16. Further enhance FDA's internal processes for responding to and investigating reports of suspected counterfeit products.

D. Education and Public Awareness

The Task Force heard from many sources that there is a great need to increase awareness and education of stakeholders and the public concerning counterfeit drugs. The following options, based on what we have heard, address these issues:

17. Increase the efforts of the FDA, other government agencies, and appropriate private sector partners to educate consumers and health care professionals on how to reduce the risk of obtaining counterfeited drugs before an event occurs. Helpful messages could include: (1) what is a counterfeit drug and why U.S. consumers and health care professionals should be vigilant, (2) the dangers of buying drugs over the Internet or from other unknown entities, (3) good purchasing practices that will decrease the chances of encountering counterfeits, and (4) legitimate ways to obtain drugs (e.g. federal or state purchasing programs, private sector purchasing programs for low income consumers);

18. Educate consumers and health care professionals on how to identify counterfeit drugs (including how to recognize anti-counterfeiting technologies on packages, labeling, and drug products themselves) and what to do when they believe they have identified a counterfeit product;

19. Assure flexibility as agency officials determine their outreach approach and create a set of pre-established consumer and professional outreach plans that can be utilized if deemed appropriate (based on risk analysis) after counterfeits are detected in the stream of commerce;

20. Provide outreach efforts appropriate for the diverse elements of the U.S. drug distribution system. We find that individual strategies for educating and increasing awareness should be considered for diverse stakeholders including: consumers, pharmacists, wholesalers, repackers, doctors, nurses, the media, and public health officials. These creative strategies could take the form of public service announcements, educational fliers and communication tools that can be distributed by pharmacists and PBMs, toll-free numbers on labels; permanent messaging on appropriate industry and private group websites to establish a permanent presence, as well as many other potential tools.

21. Explore ways of improving and coordinating agency and industry messages and efforts to address and contain a counterfeit event. Though a drug manufacturer is not responsible for the creation of a counterfeit of its products, ensuring health professionals are well informed about the event and protecting the public from it should be a shared public policy goal.

E. International Issues

The task heard that counterfeiting of drugs is commonplace in many countries. The global nature of counterfeiting suggests that American stakeholders should work with foreign stakeholders to better coordinate their anti-counterfeiting efforts. The following options, based on what we have heard to date, relate to these issues:

22. Strengthen international cooperation in law enforcement efforts, identification of counterfeit products, use of anti-counterfeiting technologies, and education of stakeholders and consumers;

23. Develop global standards for (a) the packaging of final dosage forms and API's, (b) the use of tamper evident packaging, (c) product pedigrees, (d) the use of anti-counterfeiting measures, and (e) the use of track/trace technologies.

IV. Questions Related to the Potential Options for Improving Prescription Drug Security

A. Questions Concerning Technology (Options 1-9)

1. Discuss the advantages and disadvantages of unit of use packaging. Please provide any information on the economic impact of requiring unit of use packaging.

2. Should the European Union requirements be used as a model for unit of use packaging?

3. Discuss the advantages and disadvantages of using tamper evident packaging on drug products. Please provide any information on the economic impact of requiring tamper evident packaging features on these products.

4. What anti-counterfeiting technologies are currently being used? Are there any data on which technologies are successful?

5. What, if any, minimum number of anti-counterfeiting technologies should be utilized on packaging and labeling? Should technologies be utilized on all dosage forms (e.g., APIs, finished dosage forms) and products or just dosage forms and products at high risk of being counterfeited?

6. Should any specific anti-counterfeiting technologies be utilized? Should covert technologies always be utilized? Should overt technologies always be utilized?

7. Should some anti-counterfeiting technologies only be identifiable by the manufacturer and/or the FDA?

8. On what dosage forms and products should taggants, other markers, or unique characteristics be utilized? All dosage forms and products? High-risk dosage forms and products? Are there unique characteristics of products that can be utilized in lieu of taggants or chemical markers for forensic analysis?

9. What role should the FDA play in reviewing the use of (i) anti-counterfeiting technologies incorporated into the packaging and labeling, (ii) taggants, markers, and other unique characteristics incorporated into the product itself, and (iii) track and trace technologies?

10. How should "validation" of an anti-counterfeiting measure or track and trace technology be determined? Should only "validated" anti-counterfeiting measures be used? Who should do the validation?

11. Should a database, as described in Technology Option 5 be created? If so, who should develop the database? Where should it be housed? Who should have access to the data? Who should be responsible for updating and maintaining it?

12. Discuss the advantages and disadvantages and the role of track and trace technologies, in particular bar codes and RFID.

13. What are the costs and challenges involved with setting up an infrastructure for utilizing various track and trace technologies?

14. Tracking and tracing drugs and biologics throughout the drug distribution chain may result in the creation of a large database that includes tracking data from each entity that "handles" the product. Who should create and maintain such data? Where and how should the data be housed? Who should have access to the data? How can appropriate confidentiality be assured?

15. Are there additional benefits beyond the ability to detect counterfeit product that anti-counterfeiting and track/trace technologies can provide for industry, (e.g., inventory control, facilitation of product recalls, and identification of theft and product diversion)? Give specific examples.

16. Discuss the logistic, economic, and public health effects of direct shipment of product to retailers and other end users.

17. For products that are shipped directly from manufacturers to retailers, would the use of track and trace technology on those products provide any additional benefits?

18. Should all products be considered at high risk of being counterfeited? How can products at high risk of being counterfeited be identified? Which, if any, of the following criteria should be considered: (a) potential impact on public health if the product were counterfeited, (b) any history of, or the potential for, counterfeiting, tampering, or diversion of the product, (c) wholesale and retail price of the product, (d) volume of product sold, both on a unit and dollar basis, (e) the dosage form of the product, e.g., injectable, (f) approved and unapproved uses of the product, (g) current and potential misuse or abuse of the product, e.g., "street value", (h) other products in the class with a history of being counterfeited, (i) the length of remaining patent life for the product?

19. Discuss what could be included in an FDA guidance on the use of anti-counterfeiting technologies.

20. Should FDA conduct research on development or evaluation of anti-counterfeiting technologies? If so what should this research focus on? How should FDA integrate its research efforts with other public and private sector efforts?

21. Discuss what could be included in an FDA guidance on physical site security and supply chain integrity.

B. Questions Concerning Regulatory Requirements and Secure Business Practices (Options 10-13)

1. Discuss the most effective ways to achieve the goals of the wholesale distribution rule (21 CFR 203.3(u) and 203.50). Given recent or impending advances in technology, comment on the feasibility of using an electronic pedigree in lieu of a paper pedigree.

2. Discuss the advantages and disadvantages of the new Florida and Nevada requirements for wholesale distributors, including the costs involved with compliance.

3. Discuss the advantages and disadvantages of requiring a pedigree if track and trace technology is also being utilized for a given product?

4. Identify areas where the NABP Model Rules for Licensure of Wholesale Distributors could be strengthened. Please give specific language for new provisions.

5. Discuss the strengths and weaknesses of a pedigree as a means of tracking product integrity. Is there a deterrent value in having a pedigree? What is the most cost-effective approach to obtaining reliable pedigree information?

6. Discuss the advantages and disadvantages of increased penalties for counterfeiting drugs?

7. Identify areas where business practices could be changed to prevent the introduction, and facilitate the identification, of counterfeit drugs.

8. Describe the current use of designated personnel and teams to implement and monitor anti-counterfeiting measures by manufacturers, wholesalers, re-packagers, and pharmacies.

9. Comment on the advantages and disadvantages of manufacturers sharing market data with the FDA for use in identifying counterfeit products.

10. Comment on the need for FDA guidance dealing with site security and supply chain integrity in light of the importance of drug treatment for bioterrorism incidents.

C. Questions Concerning Rapid Alert and Response Systems (Options 14-16)

1. What are the advantages and disadvantages of adapting the MedWatch system for use in disseminating information about counterfeit drugs?

2. What are the current capabilities of private communication systems or networks (e.g., association list-serves, websites) for handling information about counterfeit drugs in a timely manner?

3. What current electronic communication systems or networks are being used by the private sector to share information and can they be linked with MedWatch?

4. What capabilities should a communication network have in order to be part of a counterfeit alert system? For example: Should the system be accessible to all stakeholders (e.g., pharmacies, wholesalers)? How fast should the system be able to disseminate information about suspect product? Should messaging be active? How should the system flag messages about suspect product as opposed to less urgent information? Should access be at no cost? Should all networks in the system have a uniform method of presenting and distributing information? How secure must the system be? Should access to information be selective? Should the system be capable of direct linkage to the FDA? Should the system be able to transmit educational information?

5. What are the costs associated with developing a new counterfeit alert network? What are the costs associated with adapting current systems or networks to be part of a counterfeit alert network? (In both cases, having the features listed in (d) above)

D. Questions Concerning Education and Public Awareness (Options 17-21)

1. How can FDA best assist in making sure the public knows what they need to know to help them avoid counterfeit drugs?

2. What role should the private sector, professional/trade associations and consumer representatives play in educating consumers and health professionals? Are there other groups that FDA should solicit for help?

3. How should FDA interact with various private sector and trade groups to educate consumers about the threats of counterfeits before they enter the stream of commerce?

4. What education and communication tools are available? Which will be the most effective and efficient for this effort?

5. Once a counterfeit drug is identified, what tools are available to the agency to notify potentially affected parties without inappropriately scaring other consumers from taking their medications?

6. How should these efforts be supported or funded? Is partnership with potentially affected parties appropriate?

7. Are there additional long term messages, in addition to those listed above, that the FDA should deliver to its targeted audiences? Similarly, are there additional messages that the FDA should deliver when a report of a counterfeit product is received by the agency?

E. Questions Concerning International Issues (Options 22-23)

1. What measures have foreign governments instituted (or are planning to institute) to address the problem of counterfeit drugs?

2. What global standards are needed to address the problem of counterfeit drugs? Who should develop these standards?

3. What processes will be effective in setting global standards?

V. Request for Comments

FDA seeks comment on issues related to the potential options presented here, as well as the specific questions posed above. Interested persons may submit to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, Maryland, 20852, written or electric comments by November 3, 2003. Electronic comments can be submitted to http://www.fda.gov/dockets/ecomments. Groups should submit two copies. Individuals may submit one copy. You should annotate and organize your comments to identify the specific options or questions to which they refer. To ensure timely handling, the outer envelope should clearly state the docket number, 2003N-0361.

REFERENCES

1. Profile of the Prescription Drug Wholesaling Industry. ERG. February 12, 2001

2. Florida Statewide Grand Jury Report, February 2003

3. The Prescription Drug Marketing Act Report to Congress, FDA, June 2001 http://www.fda.gov/oc/pdma/report2001/

4. NABP Model Rules

Appendix A: Table of Anti-Counterfeiting Measures

SECURITY TECHNOLOGIES

Features	Type	Description	Benefits
Overt Security Features			
Substrate			
Conventional	overt, tactile	Cotton & linen fibers; no UV fluorescence	Recognizable tactile properties (feel)
Alternate			
Laminate (paper-plastic blend)	overt, tactile	Synthetic & natural fibers	Retains some paper tactile properties
Synthetic	overt	Polymeric material	Increased durability & circulation life.
Watermark			
Registered	overt	Portrait similar to the intaglio portrait, at the same location on each note	Consumer authenticator
Overall	overt	Overall pattern not registered to a specific note location	Improves printability, does not require an open area on the note
Planchettes	overt, covert	Small tissue or polymer discs incorporated in the substrate, can carry additional covert features, e.g., fluorescence, microprint.	Consumer verification

SECURITY TECHNOLOGIES (cont.)

Features	Type	Description	Benefits
Thread			
Embedded	overt, covert	Thread indiscernible in reflected light, visible with transmitted light	Consumer authenticator, machine readable, copier reproduction difficult.
Printing	overt	Text/images on thread	Consumer authenticator
Fluorescence	covert	Fluorescent material on thread	Machine readable
Magnetic	covert	Magnetic material on thread	Machine readable
Windowed	overt, covert	Thread discernible when exposed on substrate surface	Consumer authenticator, degrades copier/scanner reproduction, machine readable
Printing	overt	Text/images on thread	Consumer authenticator
Fluorescence	covert	Carries fluorescent material	Machine readable
Optical Pigments & Dyes			
Up Converters	overt, covert	Material absorbs long wavelength radiation and re-emits at shorter wavelength, e.g., absorbs infrared radiation and re-emits as visible light or shorter wavelength infrared light	Authenticator, Consumer Authenticator, Machine Readable
Down Converters	overt, covert	Material absorbs short wavelength radiation and re-emits at longer wavelength, e.g., absorbs ultraviolet radiation and re-emits as visible or infrared light	Consumer authenticator, machine readable

SECURITY TECHNOLOGIES (cont.)

Features	Type	Description	Benefits
Inks			
Offset			
Color Gamut	overt	Printing with colors which cannot be reproduced by the four color process of current copiers and printers	Digital reprographic equipment not able to reproduce certain colors.
Color Shifting	overt	Color changes with viewing angle	Consumer authenticator, color shift hard to scan or simulate
Thermochromic	overt	Color change with temperature	Consumer authenticator
Photochromic	overt	Color shift with light	Consumer authenticator
General			
Forensic Tag	covert	Marker for forensic identification that provides a unique product source fingerprint, e.g., unique submicron security features on carrier particles or deuterated tracer materials	Authenticity test and tracking
Intaglio			
Magnetics	covert, tactile	Magnetic properties	Machine readable
Infrared	covert, tactile	Infrared active	Machine readable

SECURITY TECHNOLOGIES (cont.)

Features	Type	Description	Benefits
Other, Printed			
Digital Watermark	overt, covert	A printed feature with embedded encrypted digital information that can only be read by software having the correct decryption key	Authenticator, machine readable
Latent image	overt	Variation in surface relief of an intaglio print resulting in an observable image at very low angles	Consumer verification; will not reproduce on copiers
Moire Inducing Patterns	overt	Printed patterns which cause frequency interference in low to medium resolution digital scans	Consumer authenticator, degrades imaging on copiers and low to medium resolution scanners/printers
Lenticular/Scrambled Indicia	overt	Printed, embedded image viewable with a special lens	Consumer authenticator, machine readable

SECURITY TECHNOLOGIES (cont.)

Features	Type	Description	Benefits
Other, Non-printed			
Microperf	overt	Laser perforations in a grid pattern, acts as an optically variable device, visible when viewed in transmitted light at 90° angle	Consumer authenticator, cannot be scanned, difficult to reproduce
Holograms	overt	3D-like images	Consumer authenticator, machine readable
Optically Variable Devices	overt	Devices that change optical character via viewing angle or stimulation	Consumer authenticator, machine readable
Radio Frequency Identification Devices	covert	Electronic device that transmits, via radio frequency over a limited distance, encrypted info when interrogated, info resides in the computer chip of the RFID tag	Machine readable, tracking
Passive	covert	No battery, power drawn from reader	Machine readable, short distance tracking
Semi-passive	covert	Battery powers chip, transmitting power drawn from reader	Machine readable
Active	covert	Self-contained battery for chip and RF transmissions	Machine readable

SECURITY TECHNOLOGIES (cont.)

Features	Type	Description	Benefits
Other, Taggants			
Marker tags	overt, covert	Components which can be added to fibers, planchettes, inks, thread; and provide specific properties such as fluorescence	Authenticator possible, machine readable
Organic vapor	overt	Unique odor signature, e.g., perfume	Consumer authenticator, machine readable
Micro-barcode tag	covert, overt	Color layered barcode patterns on 20 - 600 micron size particles, which can hold information	Authenticator, tracking, machine readable
Organic tag	covert	Organic chemical markers, such as DNA, that can be detected by instrument or animals, e.g., quadrapole, ion mass spectrometry	Machine readable, tracking
Inorganic tag	covert	Inorganic chemical markers that can be detected by instruments, e.g., magnetometers, x-ray units, IR/UV/visible spectrophotometers	Machine readable

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