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February 24, 2006

Dockets Management Branch
(HFA-HFA-305)
Food and Drug Administration
5630 Fishers Lane
rm. 1061
Rockville, MD 20852

Re: Docket Number 2005N-0510; FDA Anti-Counterfeit Drug Initiative; 71 Federal Register
1759; January 11, 2006

Dear Sir/Madam:

The following comments on the Food and Drug Administration's (FDA) Anti-Counterfeiting Drug Initiative are submitted on behalf of the Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA welcomes the opportunity to respond to the Food and Drug Administration's (FDA) request for comment on the use of Radio Frequency Identification (RFID) tag technology to secure the safety of America's pharmaceutical supply chain. PhRMA represents the country's leading research-based pharmaceutical and biotechnology companies. Our member companies are devoted to inventing medicines that allow patients to lead longer, happier, healthier, and more productive lives. In 2004, our members invested over \$38 billion in the discovery and development of new medicines.

PhRMA member companies have a strong interest in ensuring the supply chain that moves drugs from the manufacturer to the patient is safe and secure. Our members also manufacture these products following exacting standards and extensive quality systems to assure that our innovative medicines provide consistent positive health outcomes. Even the most innovative medicines cannot help the patients who need them if those medicines are compromised by breakdowns in the distribution system, including diversion and counterfeiting. PhRMA member companies are committed to embracing new technologies as a means of protecting the integrity of the American drug supply. PhRMA has both general comments on the use of RFID technology and specific answers to the questions that FDA posed in the Federal Register statement. These are outlined in the following sections.

GENERAL COMMENTS

As has been noted by FDA and stakeholders there is no single "magic bullet" that will prevent counterfeiting. The report issued by the FDA on February 20, 2004 entitled "Combating Counterfeit Drugs: A Report of the Food and Drug Administration" highlighted the following measures:

- Securing drug product, it's packaging and movement of product
- Enhancing regulatory oversight and enforcement
- Increasing penalties for counterfeiters
- Heightening vigilance and awareness of counterfeit drugs
- Increasing international collaboration

Pharmaceutical Research and Manufacturers of America

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Through the use of innovative packaging technologies and improved business practices, providing regulatory clarity, and increased enforcement against counterfeiters, the security of the pharmaceutical supply chain can be strengthened. Even the use of RFID technology will not fully solve the problem unless corresponding business practices are changed with the introduction of this technology. It is important for FDA to remember that an RFID encoded package serial number only authenticates the packaging; it does not and cannot be used in the absence of other business practice changes to attest to the purity, potency, and safety of the drug product in the package.

The pharmaceutical industry has worked closely with other industry stakeholders, including wholesalers, pharmacies and federal and state regulators, to examine and test the feasibility of establishing a nationwide electronic pedigree system to secure the nation's drug supply. PhRMA companies have ongoing pilots involving the labeling of targeted packaged pharmaceuticals with RFID tags. Some labeled pharmaceutical packaging has entered commerce already as a result of these pilots and others are expected soon.

However, widespread introduction of serialized pharmaceutical packaging into the supply chain requires many processes as well as technological changes. Manufacturers applying serial numbers via bar codes or RFID tags are only the start. Each supply chain partner downstream from the manufacturer must be required to authenticate the serial number to ensure true electronic track and trace.

Standards must be developed and incorporated into the technical solutions used to secure the supply chain and insure interoperability across the various supply chain parties. These standards must be adopted by all supply chain parties before electronic track and trace can be fully implemented. This process of adopting mass serialization, authentication, and electronic track and trace, and the accompanying change in business practices will be a very large, complex endeavor. A phased in approach will be the only way that change of this magnitude can be successfully implemented. The industry must be given sufficient time to work together to establish an appropriate time frame for achieving the goal of improving supply chain security.

PhRMA issued a White Paper last year outlining how electronic authentication technologies can lead to a safer drug distribution system. The complete version of this White Paper is attached as Appendix One of this communication. Serialization of pharmaceutical packaging can be used to authenticate whether the package unit originated with the identified manufacturer. The serial number can be encoded in either an RFID tag or a two dimensional bar code, both technologies are machine readable. Barcodes such as 2-D DataMatrix offer advantages in terms of experience and cost while RFID offers the advantage of not requiring a line of sight reading. In addition, there are still product stability issues to consider from the exposure of RFID tagged product to radio frequency energy.

The use of electronic authentication to secure the drug supply chain is straight forward and differs markedly from and should not be confused with the use of paper or electronic pedigrees as called for under the Prescription Drug Marketing Act (PDMA)¹. The following schema outlines the approach for implementation:

¹ 21 USC §§ 331(t), 333(b), 353(c)-(e), and 381; implementing regulations can be found at 21 CFR § 203.50

1. The manufacturer places a machine readable serial number on the packaging. The minimum data elements are a) the serial number and b) a pointer to the database where the necessary information to identify the specific pharmaceutical is contained. For the purposes of preventing counterfeiting or diversion the NDC number or any other product identifier is NOT required on the RFID tag or bar code, it is resident in the database as is the lot number.
2. The first recipient of the packaged pharmaceutical electronically authenticates the serial number. A query to the database authenticates the number as being assigned to that particular package unit. The recipient's business information and transaction date (as per FDA regulations at 21 CFR § 203.50 (a)(6 & 7)) can be electronically recorded in the database.
3. Step 2 is repeated for all subsequent transactions. If a recipient of the pharmaceutical package does not authenticate the serial number according to the above business practice, it will not be registered in the database. When the next recipient attempts to authenticate, the database query will respond with a message that the unit was not properly authenticated by the previous trading partner. Further distribution should cease until the cause for non-authentication is identified. Unlike the paper pedigree paradigm outlined in the current FDA regulations, the information does NOT need to be passed on to trading partners as long as proper authentication takes place following a transaction.
4. The serial number is closed out at the point of dispensing. Subsequent queries to the database for that particular serial number will result in a response that it is non-authentic.

There may be other uses of the above described authentication technology that are not related to supply chain security and safety. These should be the subject of separate discussions between trading partners and are unrelated to FDA's interest in anti-counterfeiting technologies.

There still remains a significant amount of work that needs to be done in order to move towards an electronic drug authentication system. Standards for mass serialization must be finalized. A proper assessment of the read failure must be done as implementation of the technology as described above argues for as close to a 100% success rate in reads for serialized pharmaceuticals. Product that cannot be authenticated will be presumed counterfeit unless other systems are in place. In addition, there will be a tremendous amount of validation activities that will be required for start-up of these systems within manufacturing environments requiring a high degree of assurance that they will perform as intended. There have been some reports that the read rate for RFID tagged biologicals, liquids, and metal packaging fall well short of this goal. Business and data exchange practices must be put into place. The supply chain must be ready to embrace the technology in a timely manner. In addition, the scope of products that will be mass serialized must be defined. The PhRMA white paper suggests the focus should be on "targeted" pharmaceuticals that the manufacturer believes to be at a defined risk for counterfeiting or diversion. As PhRMA noted at the public meeting there also needs to be a better engagement with the generic drug industry on this topic. While generic drugs may not be the primary subject of counterfeiting, a number DEA controlled narcotic substances are generic and may be subject to diversion. PhRMA notes that the PDMA was passed by Congress to address both counterfeit and diverted drugs. The security of the supply chain clearly extends to such products.

The PhRMA white paper suggests focusing on dispensing site authentication as a first step with the following seven steps as a way to move forward in this area.

1. All package units of targeted prescription medicines should contain a machine- readable serial number that includes the company identifier. The applicable package-level to uniquely serialize includes the pallet, case, and item level.
2. The machine- readable code can include bar codes, such as linear bar code (space permitting), two dimensional DataMatrix, or RFID tags. The chosen code should be robust and reliable in terms of readability and cost effective.
3. Standards for serialization, tag data, and frequencies (in the case of RFID) must be developed in accordance with packaging hierarchy.
4. An appropriate information technology (IT) infrastructure should be constructed that will allow the dispensing site, and other trusted parties, to query through a central data portal. Data will be routed to the distributed database where information on the package unit in question is kept. The dispensing site will receive a real-time signal back that the identification number is authentic for the product in question.
5. Electronic authentication should focus initially on the end-user dispensing site, but is not intended to exclude other supply chain participants. Targeted pilots should also be undertaken by the pharmaceutical industry with the goal of furthering the development of electronic pedigrees.
6. Operating rules must be established regarding the point and time of authentication. Following dispensing of the package unit (or the opening of a container containing multiple dispensing amounts) steps should be taken to prevent the subsequent illegal use of that unit's serial number.
7. Following successful demonstration of the viability of dispensing site authentication, this technology can be added to other partners in the supply chain, adding another tool to assure authentic pharmaceutical product flow from the manufacturer to the end dispensing site.

SPECIFIC COMMENTS ON QUESTIONS POSED BY FDA

II.A. Implementation of RFID

FDA poses the question about what types of incentives are needed for widespread adoption of RFID in the drug supply chain. As noted in the PhRMA White Paper, 2-D barcodes such as DataMatrix offer a viable alternative to RFID technology and should not be dismissed out of hand. The critical issues are not related to incentives but development of the technology and the necessary decisions regarding how the technology will be utilized and how broadly it will be deployed. Standards for tag information content and frequency must be developed and agreed upon. Robustness of the tags and an evaluation of the readability are critical to implementation. A read rate approaching 100% will be required if authentication technology is to be adopted on

a widespread basis. The authenticity of a package unit is questionable if the dispensing site cannot get an accurate read from the RFID tag.

The IT infrastructure must be put into place to record the serial numbers and respond to authentication queries. Implementation of an electronic pedigree requires registration and tracking of individual transactions. RFID readers must be installed at all dispensing sites, including hospital pharmacies, and trading partners for full implementation. With approximately 80,000 dispensing sites in the US, this will be a significant technology investment from just this one sector. An analogous example of the difficulty of adoption is the slow adoption within hospitals to read unit-dose pharmaceuticals labeled with a barcode embedding the NDC number. This comes after FDA finalized a regulation that promises to reduce medication errors in such settings. Only a fraction of hospitals have the capacity to read these barcodes.

PhRMA believes that FDA should be actively involved with the various groups working towards implementation so that they are informed about the progress of technological development. Through such interactions, FDA will understand what issues require resolution and obtain a better understanding of the timeline technology adoption to better secure the supply chain. It may also confirm PhRMA's contentions that the proposed adoption pathway provided by the white paper provides a path that meets initial objectives that best addresses concerns such as database and privacy issues. Longer term, these systems may be upgraded to meet today's vision since the IT infrastructure should be the same.

It is important for FDA to recognize that the current pilots are limited in scope and costly to implement. Implementation of these small scale efforts have also been time consuming, thus arguing against an early widespread adoption. Companies will be making final decisions on the extent they use RFID tags based on the practical experienced gained during the pilots. There is no supply chain commitment at this point in time to moving towards widespread use of RFID. However, PhRMA is committed to continue working with the FDA on any or all of the measures outlined in the report with the goal of best protecting the public with most effective solutions.

II.B. RFID Standards Setting

PhRMA supports the continuing role of EPCglobal in this arena. PhRMA is an affiliate member of EPCglobal and many PhRMA companies are taking an active role in the standards setting process. EPCglobal has active participation from all the pharmaceutical industry, healthcare products distributors and dispensers of medicines as well as key vendors and consultants. EPCglobal is working towards the establishment of a public open standard that all can use.

FDA and other applicable Federal agencies such as the Drug Enforcement Administration (DEA), should be active participants in these ongoing activities. While PhRMA does not believe FDA should lead these efforts, FDA's input is necessary to ensure that standards meet existing regulatory requirements, if any.. Once the standards are finalized and in place they will be used by the pharmaceutical industry to serialize packaging. PhRMA is reluctant to call for incorporation of the standards into regulation at this point in time as it is unclear from a technical implementation how long lived they will be.

II.C. Specific Drug Supply Chain RFID and E-pedigree Issues

1. *Mass Serialization* – Number conventions and the need for inclusion of the NDC number in the RFID tag are under active discussion. As noted in our general comments the inclusion of the NDC number is not necessary for implementation of a drug authentication system. Discussions on the use of the NDC in the RFID tag are ongoing. PhRMA is concerned about FDA's question about "widespread mass serialization." From a drug safety perspective relative to the potential introduction of counterfeit drugs into the supply chain, it may be necessary to serialize only certain products, at least initially. Especially given the high costs of mass serialization, it may not be feasible to serialize all products with RFID tags.

2. *Universal Pedigree Fields* – One of the key reasons for the rise in differing state regulations regarding drug pedigrees is that FDA has not yet implemented the federal regulations at 21 CFR §203.50. The absence of this simple solution has prompted state action in this area. PhRMA strongly supports implementation of the FDA's pedigree rule as an effective interim step to combating counterfeiting while electronic authentication solutions are implemented. PhRMA believes the data elements specified in 21 CFR § 203.50 (a)(1) through (a)(5) are routinely provided on shipping orders from the manufacturer (along with the business name and address of the manufacturer, data element 6). The remaining elements, including transaction date, are completed by trading partners as the packages move through commerce. Certainly this information can be readily stored in a computer database and a pedigree built with each transaction if necessary. However, as PhRMA noted earlier, adopting electronic authentication as a common business practice by all trading partners may negate the need for passing a pedigree forward. The transaction record or pedigree would only need to be looked at if a specific question arose regarding the authenticity of that package unit.

It is possible to create a system capable of generating and passing a pedigree between trading partners. This is independent of the use of serialization and is built upon the paper pedigree paradigm.

3. *Data Management and Security* – PhRMA supports a distributed database model for storing serialized information. A company held database may prove to be more secure than a centralized database as the company can set specific access rules for data exchange. Distributed database queries should go through a central gateway in much the same way that the Internet directs one to many URLs. A segment of the serial number would provide direction to the database for the query. While it is unclear at this time whether there will be a need for electronic signature, PhRMA supported an effort which has led to a secure electronic signature that can be used on an as needed basis. More information on this can be found at www.safe-biopharma.org.

II.D. *Privacy Issues*

EPCglobal has established a Public Policy Steering Committee and PhRMA is an active participant in this group. The group is currently assessing consumer familiarity with RFID technology and the value that it can add in securing the safety of the drug supply chain. Under the PhRMA model for drug authentication there is no privacy issue as the RFID tag contains no information identifying the drug. That information is resident in the database which will only be accessible to authorized users.

III.A. 1999 PDMA Final Rule

The Prescription Drug Marketing Act of 1987 (PDMA) was an important piece of consumer legislation passed as a result of Congressional concern that the then-existing integrity of the distribution system for prescription drugs was insufficient to prevent the introduction and eventual resale of substandard, ineffective, or counterfeit drugs. It strengthened the Federal Food, Drug, and Cosmetic Act by establishing a closed distribution system in the U.S., requiring establishment of a chain of custody.

Given the serious threats to the U.S. drug supply that exist today, PhRMA does not believe that FDA and the various stakeholders have the luxury of waiting for a track and trace system to become operational before implementing a pedigree requirement. For this reason, PhRMA supports the implementation of a paper pedigree system as an interim measure while an electronic track and trace system is being developed.

PhRMA believes that implementing a pedigree requirement, even a system relying on paper records, is the single most effective action FDA could take to combat prescription drug counterfeiting in the short term. Congress recognized this in the late 1980s when it enacted a pedigree requirement as part of the PDMA. The PDMA was an important piece of consumer legislation passed as a result of Congressional concern that the integrity of the then-existing distribution system for prescription drugs was insufficient to prevent the introduction and eventual resale of substandard, ineffective, or counterfeit drugs. The primary goal of the pedigree requirement is to ensure that the U.S. drug supply remains a closed system by preventing the introduction of counterfeit medications into the supply chain. The pedigree requirement accomplishes this goal by establishing a legal chain of custody for each pharmaceutical product that permits purchasers to assure themselves that the product originated from the original manufacturer.

While the U.S. drug supply remains the safest in the world – in large measure because of the protections enacted by the PDMA – the risks that Congress identified in 1987 have only grown in recent years. As FDA knows, the counterfeiters have become increasingly sophisticated and dangerous, and the health risks from counterfeit drugs have grown. There is even evidence that organized crime has taken an interest in the shadow market for prescription drugs and has begun establishing well-funded and sophisticated rings to manufacture phony life-saving medications, such as cancer and AIDS therapies, used by the most vulnerable patients.

Although FDA finalized regulations implementing the pedigree requirement in 1999, these regulations (which are set forth at 21 C.F.R. §203.50) have been stayed four times by FDA. As a result, this potent weapon against counterfeit drugs remains unused and in administrative limbo almost *twenty years after Congress originally enacted it*. PhRMA believes that, in light of recent, serious threats to the U.S. drug supply, this situation is no longer tenable, and the pedigree requirement must be implemented immediately. In order to combat this growing public health threat, FDA should use all of the resources at its disposal, *including the pedigree requirement*.

While the existing statutory and regulatory requirements certainly can be improved (by, for instance, requiring authorized distributors of record (ADRs) to pass pedigrees), PhRMA believes that the final rule promulgated by the FDA is an accurate reflection of Congressional intent and

will provide strong deterrence against counterfeiters. See 21 C.F.R. §203.50. PhRMA acknowledges that the pedigree requirement is not a “magic bullet” but believes it will throw up a powerful roadblock against counterfeit drugs, making it significantly more difficult for counterfeiters to breach the supply chain and increasing the likelihood that, if they attempt to do so, they will be identified and caught. Indeed, pedigree papers reportedly were responsible for tipping investigators off to a major counterfeiting ring operating in Florida, leading to the indictment in July of 18 members of that ring. *Salesman Fell Into A Shadow Market*, Washington Post, p. A17 (Oct. 19, 2003). Without the information provided by pedigree papers, it is likely that this counterfeiting ring would still be operating in south Florida.

The value of the drug pedigree requirement for deterring counterfeiting activities recently was examined by a statewide Grand Jury in Florida. In a comprehensive report on the safety of prescription drugs in Florida, the Florida Grand Jury reached the following conclusion with respect to pedigree papers:

Pedigree papers, when verified through due diligence, are the cheapest, easiest and most effective way to prevent diverted or counterfeited drugs from entering the marketplace.

First Interim Report of the Seventeenth Statewide Grand Jury, Case No. SC02-2645, at 34 (Grand Jury Report). PhRMA agrees with this position and with the Grand Jury’s further conclusion that a pedigree requirement should be implemented and enforced.

PhRMA acknowledges that paper pedigrees can be forged and counterfeited. However, PhRMA agrees with the Florida Grand Jury that this “is not a reason to ignore them as the [wholesaler] industry asserts; to the contrary, it is why they must be verified.” Grand Jury Report, at 29-30. If a pedigree paper is forged, the prospective purchaser can detect this quickly and cheaply through routine due diligence. PhRMA believes that FDA has authority under the PDMA to require wholesalers to verify the accuracy of the information on a drug pedigree before completing a purchase. However, even in the absence of binding regulations, PhRMA believes that evolving business standards and liability concerns will force wholesalers to use due diligence to verify pedigree information.

Moreover, pedigree papers provide an additional hurdle for counterfeiters to overcome and an additional opportunity for legitimate wholesalers and law enforcement officials to identify counterfeiters. Recent events in Florida illustrate the importance of paper pedigrees in detecting counterfeit drugs. The Washington Post recently reported that a counterfeiting ring operating in Florida was initially identified when a prospective purchaser became suspicious about the information contained on a forged pedigree paper. The purchaser notified law enforcement, which seized thousands of dollars worth of counterfeit drugs and brought indictments against 18 members of the counterfeiting ring. Accordingly, the possibility of forged pedigree papers is not a valid reason for failing to implement the current regulations. On the contrary, forged pedigree papers provide an additional opportunity to identify counterfeiters and to block counterfeit drugs from entering the drug supply, especially if wholesalers exercise the due diligence contemplated by the PDMA.

Despite the clear deterrent value of paper pedigrees, FDA has failed to implement its final pedigree regulations. This is due, in part, to concerns that the PDMA does not require

authorized distributors of record (ADRs) to pass pedigree information to their customers. While this clearly is a weakness in the current statute that needs to be addressed, it does not justify FDA's wholesale refusal to implement any pedigree requirement whatsoever. If FDA is concerned that secondary wholesalers will not be able to obtain information tracing the drug back to the manufacturer because of the refusal of ADRs to pass on this information, FDA can exercise its enforcement discretion in this area. In other words, FDA can commit that it will not take enforcement action against a wholesaler if the wholesaler 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. PhRMA believes that this would be an appropriate exercise of FDA's enforcement discretion to facilitate a functional and effective pedigree system while FDA works with Congress to address the weakness in the current law.

PhRMA also believes it would be appropriate for FDA to encourage ADRs to pass on pedigree information voluntarily. PhRMA believes that ADRs should not frustrate the pedigree system by refusing to pass on needed information to secondary wholesalers and calls on the wholesale industry to pass on all necessary pedigree information.

In sum, PhRMA believes that paper pedigrees, combined with routine due diligence, provide the most cost-effective approach available at this time for obtaining reliable pedigree information. Although electronic track and trace systems ultimately may prove more cost-effective, these systems realistically cannot be implemented throughout the distribution system for at least five years. In the interim, PhRMA agrees with the Florida Grand Jury that "[p]edigree papers, when verified through due diligence, are the cheapest, easiest and most effective way to prevent diverted or counterfeited drugs from entering the marketplace." Grand Jury Report, at 34. PhRMA thus urges FDA to implement its regulations immediately as an interim step while electronic track and trace systems are being developed.

PhRMA trusts these comments are useful to FDA as they move forward in finalizing a report to the Commissioner on the scope, usefulness and barriers to the implementation of RFID technology.

Sincerely,

A handwritten signature in cursive script, appearing to read "Alan Goldhammer".

APPENDIX ONE

May, 2005

Electronic Authentication of Pharmaceutical Packaging and the Assurance of Public Safety: Position of the Pharmaceutical Research and Manufacturers of America

Overview

This White Paper establishes the position of the Pharmaceutical Research and Manufacturers of America (PhRMA) on the use of electronic authentication technologies, such as two-dimensional bar codes and radio-frequency identification (RFID) tags, to secure the U.S. drug supply against counterfeiting threats. PhRMA issues this White Paper to engage patients, trading partners, state regulatory authorities and the Food and Drug Administration (FDA) in discussions that will lead to a safer and more secure pharmaceutical supply chain.

In its final report on Combating Counterfeit Drugs issued on February 18, 2004 (Final Report), FDA concluded that the use of RFID technology to establish an electronic pedigree represented the "single most powerful tool available to secure the U.S. drug supply." Since then, the pharmaceutical industry has worked closely with other industry stakeholders, including wholesalers, pharmacies and federal and state regulators, to examine and test the feasibility of establishing a nationwide electronic pedigree system to secure the nation's drug supply.

PhRMA recognizes the goal of implementing a fully operational RFID track and trace system that effectively combats counterfeiting is still many years off. While this process should be accelerated, the immediate danger of counterfeit medicines entering the U.S. supply chain argues for prompt implementation of the pedigree requirements of the Prescription Drug Marketing Act (PDMA). PhRMA reiterated this position at the FDA Part 15 hearing in October 2000. This White Paper does not change PhRMA's belief in the necessity of moving forward with that requirement while progress is made on the technology front. PhRMA also supports the states' efforts at immediate implementation of paper pedigree requirements.

In addition however, and in light of practical experience not available in early 2004 and the complexity of any electronic pedigree solution, PhRMA has concluded that it is important to make progress in adopting electronic mechanisms that will permit the real-time authentication of prescription pharmaceutical packaging directly at the dispensing level. The implementation of an RFID-based electronic pedigree system is likely to be complex and not fully achievable for five or more years. Current use of RFID tags is limited by robustness and the impact on the affordability of medicines.

The dispensing site is a critical link in the drug distribution chain, since it is the last stop before a drug is dispensed to a patient. Authentication of drug products at this juncture would have a direct, immediate and lasting impact on patient safety. This PhRMA proposal does not preclude other trading partners from authenticating pharmaceutical packaging, and in fact PhRMA encourages this as a means of migrating towards an electronic pedigree. PhRMA believes that

the goal of real-time authentication at the dispensing site can be accomplished in the near term using mass serialization and available electronic technology, such as bar coding or RFID tags.

Focusing on the dispensing site permits electronic authentication systems to be implemented in a timely manner, benefiting patients in the earliest stages of development. In later stages, electronic authentication could be expanded throughout the distribution system to cover all trading partners. The resulting "electronic pedigree" essentially becomes a series of authentication steps electronically recorded in a database. PhRMA believes that the interests of patient safety in securing the drug supply are too important to delay electronic authentication at the dispensing level while extensive "electronic pedigree" systems are developed.

Background

PhRMA member companies have a strong interest in ensuring that the drugs they discover and manufacture are safe, effective and of the highest quality. This interest extends beyond the factory gates all the way to the patient, since even the most innovative medicines cannot help the patients who need them if those medicines are compromised by breakdowns in the distribution system. PhRMA member companies are committed to doing their part to protect the integrity of the American drug supply. Critical to this enterprise is the ability to verify the authenticity and integrity of the original pharmaceutical packaging unit before drug product is dispensed to a patient.

Given the complexity of the drug distribution system in the United States, this is no easy task. It has been estimated that there are approximately 80,000 dispensing sites in the United States that are supplied by a shifting group of primary and secondary wholesalers. While three major drug distributors dominate the primary market, there are a much larger number of both licensed primary and secondary distributors. Secondary buying and selling of packaged pharmaceuticals is common as a normal part of inventory adjustment; however it is often the way in which counterfeit medicines have entered the U.S. distribution system. Personal importation of small amounts of pharmaceuticals has been documented with increasing frequency. In addition, numerous Internet sites offer consumers pharmaceuticals at deeply discounted prices even though these products are of dubious origin and quality. Repackaging of pharmaceuticals takes place at a variety of levels despite the fact the manufacturer's original container/closure system has been breached and product quality may suffer as a result. Collectively, all of the above practices may create opportunities for counterfeit or diverted drugs to enter the system, thus potentially compromising the public health of patients.

Pharmaceutical companies use a variety of counterfeit resistant technologies on drug packaging and labeling to help protect the integrity of the U.S. drug supply. These include overt and covert packaging and labeling features, such as color-shifting inks, holograms, and micro-printing, as well as chemical taggants embedded in the drug product itself. These technologies provide multiple layers of security that make drug products more difficult for counterfeiters to reproduce accurately. They also are useful for assessing the authenticity of drug products already identified as "questionable."

It is important to recognize, however, that counterfeit resistant technologies may not provide a mechanism for identifying counterfeit drugs in real time, particularly at the dispensing level. First, counterfeit resistant technologies can themselves be duplicated, often within 12-18

months, and thus need to be rotated on a regular basis. Second, neither pharmacists nor patients realistically can be expected to routinely check, or even be aware of, the wide variety of overt features used on the thousands of different drug products available through pharmacies, particularly if those features are rotated on a regular basis. Third, overt and covert packaging technologies are rendered useless if a drug product is repackaged, a practice that is common in the industry and subject to only minimal regulation. That is why the integrity of the drug supply chain needs to be protected through safeguards throughout the distribution system to prevent the entry of counterfeit drugs into the US.

Near-Term Electronic Authentication Leads to an Electronic Pedigree

The use of bar coding and/or RFID technology for electronic authentication has numerous advantages. Electronic authentication is more direct, less complex, could be implemented more expeditiously, could be expanded easily, and would provide immediate safety benefits where they are most needed – to patients at the dispensing level.

Electronic authentication at the dispensing level provides a direct means of determining in real-time whether a particular packaging unit is authentic (e.g., labeled by the manufacturer). This differs from a pedigree system, which is, ultimately, the recording of a series of authentications at each trade once the package unit has left the manufacturer. Because some trading partners have argued it cumbersome and unworkable, the PDMA paper pedigree regulations have yet to be implemented. As a result, states are taking the initiative to require the implementation of a paper pedigree as a condition of drug distribution in the state, prior to the availability of an electronic system, as a means to safeguard the drug distribution system. Widely available bar-coding technology and mass-serialization of packaging units can help in the authentication process at the dispensing site and by trading partners. RFID tags can replace bar coding when their robustness is demonstrated.

Initial focus on electronic authentication may be less complex in terms of required participants. Whereas an electronic pedigree system will not be effective unless widely adopted throughout the distribution system all the way to the dispensing level, electronic authentication can be effective with the active participation of manufacturers and dispensers. . However, the participation of all trading partners at this early stage is encouraged and will lead to the migration to a robust electronic pedigree system as design features can be piloted at the same time that improved protection of the drug supply is being realized.

Although FDA and some states have stated that an electronic pedigree system could be operational as early as 2007, PhRMA believes these projections are overly optimistic. Even if stakeholders could quickly resolve the complex technological, legal, regulatory and policy issues associated with establishing a nationwide, electronic pedigree system throughout the distribution chain, there are still basic scientific issues that need to be addressed, such as the readability of RFID tags at the item, case and pallet level.

Implementing electronic authentication in a stepwise fashion with a simplified information infrastructure allows technological and other issues to be resolved (e.g., tag readability), but also provides immediate safety benefits during the implementation period. Coupled with the paper pedigree system to fill in the authentication gaps, this approach may have immediate benefits and offer needed safeguards to patients who receive medications in the U.S.

Approaches that begin the migration path for electronic pedigree systems at the wholesale level and focus on the tagging of pallets and cases, rather than units, may provide great benefits to wholesalers in terms of inventory control but little or no safety benefit to patients. With electronic authentication, PhRMA proposes a migration path that begins at the manufacturers' packaging facility and ends at the most critical juncture – the dispensing site – since this is the point at which patient safety is paramount. Consequently, while electronic track and trace processes are developing throughout the distribution chain with the building out of the necessary Information Systems, patients will be benefiting from the real-time authentication of drug packaging units at the dispensing site.

PhRMA Proposal for Implementing Electronic Authentication

In order to move towards early adoption of electronic authentication, PhRMA proposes the following steps:

1. All package units of targeted prescription medicines should contain a machine- readable serial number that includes the company identifier. The applicable package-level to uniquely serialize includes the pallet, case, and item level.
2. The machine- readable code can include bar codes, such as linear bar code (space permitting), two dimensional DataMatrix, or RFID tags. The chosen code should be robust and reliable in terms of readability and cost effective (e.g., not materially affect the affordability of the medicine).
3. Standards for serialization, tag data, and frequencies (in the case of RFID) must be developed in accordance with packaging hierarchy.
4. An appropriate information technology (IT) infrastructure should be constructed that will allow the dispensing site, and other trusted parties, to query through a central data portal. Data will be routed to the distributed database where information on the package unit in question is kept. The dispensing site will receive a real-time signal back that the identification number is authentic for the product in question.
5. Electronic authentication should focus initially on the end-user dispensing site, but is not intended to exclude other supply chain participants. Targeted pilots should also be undertaken by the pharmaceutical industry with the goal of furthering the development of electronic pedigrees.
6. Operating rules must be established regarding the point and time of authentication. Following dispensing of the package unit (or the opening of a container containing multiple dispensing amounts) steps should be taken to prevent the subsequent illegal use of that unit's serial number.
7. Following successful demonstration of the viability of dispensing site authentication, this technology can be added to other partners in the supply chain, adding another tool to assure authentic pharmaceutical product flow from the manufacturer to the end dispensing site.

PhRMA is prepared to collaborate with trading partners and Federal and State policy makers to achieve the near term goals set forth in this White Paper with the goal of establishing uniform standards throughout the United States.