Healthcare Distribution Management Association

May 19, 2008

Division of Dockets Management (HFA–305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Standards for Standardized Numerical Identifier, Validation, Track and Trace, and Authentication for Prescription Drugs; Request for Comments; 73 Fed. Reg. 14988 (March 20, 2008) [Docket No. FDA–2008–N–0120]

Dear Docket Officer:

The Healthcare Distribution Management Association (HDMA) appreciates this opportunity to provide public comments on the Food and Drug Administration's (FDA) Request for Comments, Standards for Standardized Numerical Identifier, Validation, Track and Trace, and Authentication for Prescription Drugs, 73 Fed. Reg. 14988 (March 20, 2008). This request for public comments arises from FDA's implementation of the Food and Drug Administration Amendments Act of 2007 (FDAAA).

HDMA is the national association representing primary, full-service healthcare distributors. Each day, the member companies of HDMA are responsible for ensuring that more than 13 million prescription medicines and healthcare products are safely delivered to 144,000 pharmacies, hospitals, nursing homes, physician offices, clinics, government and other providers in all 50 states. This essential public health function is provided with tremendous efficiency, saving the nation's healthcare system nearly $34 billion each year. HDMA and its members are the vital link in the healthcare system, working daily to provide value, remove costs and develop innovative solutions to deliver care safely and effectively.

Below is a synopsis of the central points that HDMA feels are most important when evaluating standards and technology for a standardized numerical identifier, validation, track and trace and authentication for prescription medicines:

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- **Supply Chain Security**: HDMA and our members have taken a strong stand to combat criminal counterfeiting, and we continue to support ongoing efforts to strengthen pedigree requirements using innovative new technologies, on behalf of patient safety and supply chain security. We believe that technologies that can track and trace individual units of medication from the beginning to the end of the supply chain hold the most promise for continued safety advances. Such technologies can link each unique package of medicine to electronic information, effectively documenting chain of custody information throughout the supply chain. Linking the physical product using a unique identifier with electronic information creates added levels of visibility and accountability that will help prevent counterfeit and diverted product from entering the supply chain.

- **Uniform National Standards**: Patient safety is enhanced with greater uniformity of pedigree requirements, standards and technologies. Uniformity is needed both to further secure our national supply chain, and also to support ongoing efforts to deploy compatible and interoperable track-and-trace technologies in a systematic way, across all 50 states. Further, a patchwork of state laws and regulations has negatively affected efforts to research and implement the use of item-level serialization with track and trace, as supply chain partners create unique systems on a state-by-state basis. We support a national standard for item serialization and track and trace to clarify implementation requirements and focus industry attention and resources on a single path.

- **Specific and Interoperable**: Uniform national standards for item-level identification of prescription medicines and an interoperable track-and-trace system should be as specific as possible. Existing and developing standards may require strict FDA guidance in terms of how those standards should be used to meet U.S. requirements. The GS1 standard for item-level serialization of medicines, for instance, allows for the use of the drug's National Drug Code (NDC) number as part of the unique identifier. HDMA believes the inclusion of the NDC number should, in fact, be mandatory in order to maintain a consistent numbering scheme across the industry. Other standards may require similar guidance.

FDA should also recognize that while much of the U.S. healthcare industry is pointing to

GS1 Healthcare as the source of standards for serialization, track and trace, bar code and Radio Frequency Identification (RFID), it is an international organization developing standards for use in many countries and for many industries. Not all elements of the appropriate standards meet the needs of current U.S. laws for pedigree and track and trace, including the Prescription Drug Marketing Act (PDMA) and requirements in California and Florida. These requirements are focused on chain-of-custody documentation, not on reimbursement or other priority issues across the globe.

- **Preferred Technology**: HDMA recommends that FDA include provisions for a single, non-line-of-sight technology, such as RFID, to serve as the primary data carrier. HDMA also recommends that FDA provide for a single secondary data carrier, the two dimensional (2D) barcode, to serve as backup. Non-line-of-sight technology is recommended as the primary data carrier because it is more secure than other technologies currently available. Alternative technologies are easier to duplicate or otherwise falsify. Non-line-of-sight technology also facilitates the rapid capture of information, and is generally more operationally efficient for the high-volume, high-throughput operations of the typical healthcare distributor. In addition, non-line-of-sight technology is potentially more accurate because it does not require the extra, manual step of repositioning the product for scanning as it enters or exits the facility. HDMA strongly recommends against establishing more than one primary data carrier. The added complexity of implementing a track–and-trace system with multiple forms of data carriers may delay implementation or undermine the intent of creating an even more secure supply chain.

Also attached are HDMA's responses to the individual questions posed in the Federal Register notice. We ask that FDA take particular note of our responses to the questions regarding "validation" and "authentication". The use of these terms in FDAAA has created some confusion among those familiar with efforts to develop standards for standardized numerical identifiers and track and trace in the prescription medicine supply chain. The terms "validation" and "authentication" usually are not related to standardized numerical identifiers and the tracking and tracing of prescription medicines. They also have little practical application to at least some components of the supply chain. We discuss these concerns in more detail in the attachment.

We have also attached for inclusion in the record, HDMA's "Baseline Technical Recommendations for Compliance with Requirements of California's SB 1476 (2006)." These recommendations were prepared to assist supply chain partners in findings ways to comply with the requirements of California law, SB 1476. We believe these recommendations may be useful to FDA as the FDAAA and SB 1476 contain similar elements; specifically, SB 1476 requires that prescription medicines move through the supply chain with a pedigree that tracks each item using a "unique identification number" in an interoperable electronic system at the smallest package level received by the pharmacy.

Finally, HDMA has two requests for further follow-up as the agency continues its efforts to implement FDAAA. We make these requests in an effort to maximize the opportunities for further securing the supply chain that FDAAA offers.

- First, HDMA urges FDA to publish the standards the agency is contemplating, to provide industry with an opportunity to comment on them, prior to finalization. Given the numerous and substantially different businesses and industries that will be affected, and the potential for confusion, particularly regarding "validation" and "authentication", we believe it is imperative that this opportunity be offered to help ensure such standards allow for optimum efficiency and security benefits across the supply chain.
- Second, as you are aware, technologies, business requirements, patient needs and prescription medicines themselves are continuously evolving. The capabilities of criminals intending to introduce counterfeits into the legitimate supply chain may also evolve. Thus, we believe it is imperative for FDA to periodically evaluate any standards that are developed and revise them as needed. This will help ensure that the most up-to-date technologies and standards are available to support the safest, most efficient applications over time.

I would like to close by commending FDA for its leadership in addressing this important matter. HDMA and our primary distributor members remain committed to working with FDA and our supply chain partners to further ensure supply chain security, and the safe delivery of prescription medicines to patients nationwide. Although technologies are still being developed and perfected, HDMA continues to support the overall goal of uniquely tracking and tracing prescription medicines from the beginning to the end of the supply chain.

If you have any questions concerning these comments, or if HDMA can provide further information that may be helpful, please do not hesitate to contact me at 703-885-0222 / pfri@hdmanet.org or Anita Ducca, Senior Director, Regulatory Affairs & Healthcare Policy, at 703-885-0240 / aducca@hdmanet.org

Sincerely,

Perry L. Fri
Senior Vice President, Industry Relations

Attachment

cc. Ilisa Bernstein, Pharm.D., J.D.
Jeffrey Shuren, M.D., J.D.

A. Standard Numerical Identifier

1. Characteristics

a. Should the standardized numerical identifier contain recognizable characteristics (e.g., National Drug Code number) or be random codes?

There should be two components to the standard identifier: Product identity, i.e., the National Drug Code (NDC), and serial number to uniquely identify the item. No other intelligence should be built into the serial number portion of the identifier. The NDC uniquely identifies the product and is ingrained in many systems across the supply chain. Existing Global Trade Item Number (GTIN) standards allow for the encoding of NDC. The FDA should follow the GTIN standard with the NDC encoded in the GTIN. Lot/batch numbers, expiration dates, pedigree history and other data elements can be exchanged electronically between trading partners as part of a track-and-trace system. This information is not meant to be part of the identifier. The unique identifier is a reference number to data records that contain information about the product and its transaction history, enabling companies to comply with current pedigree requirements.

b. Should there be a common header for item/product segregation based on product type: biologic, solid oral dosage form, etc.? If so, please elaborate.

No. As long as the identifier contains the NDC, companies will be able to continue to reference pertinent information about the product to facilitate appropriate handling. Systems today recognize products based on the NDC and allow companies to handle them accordingly. The NDC number references associated product information that would identify whether the product is a biologic, cold chain item, controlled substance or other product requiring unique handling. The NDC also identifies the package size, (i.e., case, inner pack, unit) and we recommend including the NDC as part of the standardized numerical identifier. No other intelligence should be built into the identifier.

c. How can parties in the supply chain ensure that the numbers are unique and are not duplicated?

Assuming that the serial number is of sufficient length and is not reused for a sufficient period of time, an industry-wide standard that uses the combination of the NDC and a unit serial number to establish the identifier will ensure that

number is unique across the supply chain. The NDC is used in systems throughout the supply chain. Manufacturers should be responsible for managing and assigning serial numbers for their own products, and ensuring that serial numbers remain unique through product life, as well as for recordkeeping requirements after expiration.

d. How much value would there be in having the numerical identifier in more than one place for the product (e.g., package and pallet level)?

It is important to have a numerical identifier at all levels of packaging. The most value is to have the numerical identifier at the saleable unit level. The saleable unit is the lowest level of package available for sale to the pharmacy / dispenser or point of administration. For logistical purposes, there is also value in having a standard numerical identifier at the case level to aid in receiving shipments, case storage, shipping and inference. At all packaging levels, when appropriate, the NDC should be included in the numerical identifier. For example, as long as a case is of homogenous product, the numerical identifier should include the NDC to identify the product inside the case. If it is a case of mixed product, the numerical identifier should be a serial number to uniquely identify the various items in the case. A pallet is not a common shipping unit in the supply chain. While pallets should carry a unique identifier for logistical purposes, unit-level identification is the most critical for securing the supply chain in order to keep track of the items contained on a pallet and in a case. A pallet identifier is **not useful as the only identifier**.

The case, inner pack and salable unit each should have a unique identifier. The numerical identifier should be encoded in two different data carriers for machine reading. HDMA recommends that all levels of packaging use an RFID tag as the primary data carrier to encode the identifier. Any product using RFID should also carry a secondary, or back-up, two dimensional (2D) bar code. When using RFID, each level of packaging requires only one RFID tag because line-of-sight is not necessary to scan the tag, and it does not require manual orientation or handling to read. In addition, each tag should have a bar code backup associated with it. When using bar codes, industry guidelines such as the *HDMA Guidelines for Bar Coding the Pharmaceutical Supply Chain* should be followed.

At the case level, HDMA's preferred bar code placement, as stated in the GS1-US guidelines, is on two adjacent sides. For conveyor scanning efficiency, bar coding on the wide side of the case is desirable. HDMA recommends that the narrow side (or front) of the case (one side minimum) be bar coded for single case shelf storage. Print the secondary bar code on the narrow side of the case for ease of scanning. Inner packs and smallest salable units need only one encoded identifier, preferably RFID, with a human readable back-up.

e. Should the numerical identifier be machine readable, human readable, or both?

Both. In the healthcare supply chain, a machine-readable numerical identifier should be mandatory to enable automated data capture at all points in the supply chain. In addition, the identifier should also be human readable in the event the machine-readable numerical identifier becomes unreadable. RFID is the preferred primary machine-readable carrier because it is more secure than other technologies currently available. Alternative technologies are easier to duplicate or otherwise falsify. Non-line-of-sight technology also facilitates the rapid capture of information, and is generally more operationally efficient for the high-volume, high-throughput operations of the typical healthcare distributor. In addition, non-line-of-sight technology is potentially more accurate because it does not require the extra, manual step of repositioning the product for scanning as it enters or exits the facility. Secondary, or back-up, bar coding should be machine readable. A human-readable identifier should be included at item level whenever application is possible. This may not be practical due to available space on the existing label.

f. Should the numerical identifier include the lot number and/or batch number?

No. A standard structure that includes the NDC and a serial number in the numerical identifier is sufficient to uniquely identify an item. No additional intelligence needs to be built into the identifier. Lot/batch numbers, expiration dates, pedigree history and other data elements would be linked to the identifier starting at the manufacturer and exchanged between trading partners through the supply chain as part of a track-and-trace system. This information is not meant to be part of the identifier.

A lot number is defined as a manufacturer-specific identifier applied to a set of like products for identification back to production duration, manufacturing batch or another logical grouping of the product. Hundreds of thousands of items can have the same lot number. As those products move through the supply chain, multiple distributors and even more pharmacies could receive units of a single batch all identified with the same lot number. There is no way to uniquely identify a specific unit of that manufacturing lot, nor is there a way to uniquely verify the product's transaction history.

More precisely, a lot number does not uniquely identify one product from another in the same batch and would, therefore, be ineffective to track and trace an item in the supply chain. Further, there are no current standards for lot number schema and most products do not carry lot number in a machine-readable format.

2. Standards

a. Do standards currently exist for a standardized numerical identifier of prescription drugs?

Yes. In 21 C.F.R. Part 207, FDA sets out the requirements for assignment and management of NDC numbers. The regulations governing NDC numbers are a *de facto* industry standard for product identification, and have been included in GS1 standards for product identification. Standards also have been developed at GS1 and EPCglobal for unique serialized numerical identifiers. GS1 and EPCglobal are global standards organizations that have been working on standards for numerical identification of items in the supply chain. As the standards are developed for the global community and multiple industries, the FDA should explicitly state that a drug's NDC number should be encoded in the GTIN for use in the numerical identifier. For more information on GS1 visit www.gs1.org and for EPCglobal visit www.epcglobalinc.org. Standards are constantly being revised and must be revisited on a periodic basis.

HMDA believes our "Baseline Technical Recommendations for Compliance with Requirements of California's SB 1476 (2006)" lay out the most supportable and

operationally feasible technologies that are suitable for nationwide application. These guidelines recommend the following:

Item Level

RFID – PRIMARY Carrier

- UHF Gen 2 with a SGTIN-96 encoded EPC value per the EPCglobal Tag Data Standards V1.3, Section 3.5, with NDC.
- HF Generation 2 will be supported when standards are completed.

Bar Code – BACK-UP Carrier

- 2D ECC Data Matrix encoding AI(01) GTIN + AI(21) serial number. The GTIN should include the NDC.

Case Level – Homogenous Product

RFID – PRIMARY Carrier

- UHF Gen 2 with a SGTIN-96 encoded EPC value per the EPCglobal Tag Data Standards V1.3, Section 3.5. The SGTIN should have the NDC encoded.

Bar Code – BACK-UP Carrier

- Linear GS1 Code 128 encoding concatenated AI (01) GTIN + AI (21) serial number – for cases large enough to have linear bar codes. The GTIN should have the NDC encoded.
- 2D data matrix (ECC200) encoding concatenated AI (01) GTIN + AI (21) serial number should be used for cases too small to have a linear bar code. The GTIN should have the NDC encoded.

Case Level – Mixed Product

RFID – PRIMARY Carrier

- UHF Gen 2 with a SSCC-96 encoded EPC value

Bar Code – BACK UP Carrier

- Linear GS1 Code 128 encoding AI(00) SSCC-18

Pallet Level

RFID – PRIMARY Carrier

- UHF Gen 2 with a SSCC-96 encoded EPC value

Bar Code – BACK UP Carrier

- Linear GS1 Code 128 encoding AI(00) SSCC-18

1. If so, please describe and comment on their application and use.

- Item serialization – Currently, there has been limited adoption of the item serialization standard with use occurring primarily in pilot project work. HDMA members report that some manufacturers are moving forward with serializing products to comply with California law. We believe, however, that adoption of item identification will accelerate with the introduction of a single national standard.
- SSCC-18 – Is an existing unique identifier used for mixed cases and pallets. It is meant to identify a logistical unit and not an individual package.

2. To what extent do these standards reflect stakeholder consensus?

Standards for serial identification have been developed for all levels of packaging (e.g., item, case, pallet, etc.) through GS1. The GS1 standards development process includes committees and work groups typically made up of representatives of different stakeholder groups.

At the item level, there has been debate over whether to always include the NDC/product identity in the numerical identifier on an RFID tag. The perception is that someone could identify the product by scanning its RFID tag, without actually having to see the drug product. However, most medicines dispensed to patients are transferred to vials at the pharmacy, and would not be dispensed in the original manufacturer packaging that includes the RFID tag. Further, even if a patient was carrying a medicine in the original manufacturer packaging, the RFID tag would not contain <u>any</u> patient information. It would also be very difficult to capture information about a product carried by the patient, as doing so would require an RFID reader, access to data that would decode an NDC number,

proximity to the patient and the product, among other things. The NDC is needed in the item identifier, however, because retailers use the NDC in their pharmacy systems for multiple purposes, including reimbursement.

3. Comment on whether any of these standards should be the standard adopted by FDA.

Standards for item identification as established by GS1 should be adopted by FDA because they are the most recognized and widely used across the supply chain. They must be clarified, however, to support application of the standard for even wider-scale use as a mandatory standard. Specifically, HDMA believes the NDC must be included in the item identifier and encoded in the SGTIN. Beyond the NDC, no additional intelligence, such as lot number, should be included in the numerical identifier.

4. If yes, why? Compare this standard with other standards that exist.

GS1 standards for serialization are the most recognized in the pharmaceutical supply chain and are the result of years of work involving representatives from across the supply chain. HDMA has already referenced these standards as part of recommended guidelines for meeting requirements set by the state of California. We are not aware of any other broadly-available industry standard for item-level identification. We believe it is critical that FDA adopt a single standard that allows for interoperability across the supply chain.

5. If not, is there some aspect that could be changed to make it acceptable as the FDA standard?

6. Has this standard been adopted by other countries?

In some cases, yes, but for different purposes. Some countries have sought to use standards-based numerical systems, while others have chosen to assign their own numbers, or rely on proprietary, third-party systems. It is important to note that foreign initiatives have not always focused on chain of custody tracking requirements, such as those required in the United States.

b. Are standards in development or planned for standardized numerical identifiers of prescription drugs in the supply chain? If so, who is developing these standards and what is the timeline for completion?

Yes, the global standards organization GS1 has completed a set of standards for unique numerical identifiers. For purposes of implementation in the United States, these standards are acceptable as long as there is a consistent requirement to use the NDC as part of the unique identifier.

c. What are the elements, provisions, and particular considerations that should be included in a standardized numerical identifier of prescription drugs? Please be specific in your response and include examples, where possible.

A standardized numerical identifier should include only the NDC and item serial number to uniquely identify the item. No intelligence, such as a lot number, should be built into the serial number portion of the identifier. The standard numerical identifier should be able to be encoded onto a non-line-of-sight data carrier in a standard, interoperable format. For example, the NDC and item serial number would be encoded on an RFID tag in a standard format, and incorporated in the packaging for that item.

d. Please comment on implementation of standardized numerical identifiers of prescription drugs in the U.S. supply chain.

The NDC is one standard product identifier that has been in use since the 1972 Drug Listing Act. It is presented in both human-readable and bar code form on most pharmaceutical cases, inner packs and items in the United States. Serialization standards also have now been developed for use in the tracking and tracing of medicines in the supply chain.

To effectively track and trace items in the supply chain, they must be uniquely identified at the lowest saleable unit. Without the ability to uniquely differentiate individual packages of the same item in the supply chain, it is impossible to verify the track-and-trace history.

Currently, there has been limited adoption of the item-serialization standard, with use occurring primarily in pilot project work. HDMA members report that some

manufacturers are serializing products to comply with California law. HDMA believes, however, that adoption of item identification will accelerate with the introduction of a single, national standard.

e. Please comment on any technical or information technology concerns related to a standardized numerical identifier.

In working toward implementation of a numerical identifier, there are a number of challenges, which we believe can be overcome with time, resources and exploration. For example:

- Only very few products exist today that are uniquely serialized at the unit level. This is a challenge because distributors are dependent on their suppliers to help facilitate implementation, and we do not yet have enough data to build solutions for our pharmacy customers to test.

- Today, the solutions we are building have not been built out to scale. With a limited number of products, and in limited transaction sets, technology development is progressing; however, there is no way to know what technical difficulties may arise when we reach a more realistic scale of product to work with.

- Finally, distributors' position at the center of the supply chain makes implementation of a standard identifier impossible unless our upstream trading partners can meet the serialization requirements, and our downstream customers are also able to use the identifier.

f. Comment on any ''lessons learned'' from foreign experience with standardized numerical identifiers.

Some countries have sought to use standards-based numerical systems, while others have chosen to assign their own numbers or rely on proprietary, third-party systems. It is important to note that foreign initiatives have not always focused on chain of custody tracking requirements, such as those required in the United States.

3. Economic Impact

a. What are the usual practices and associated costs that now exist for applying bar codes and other technologies for standardized numerical identifiers on packages and pallets?

In practice, a standard identifier at the unit, inner pack and case level is applied at the point of manufacture. HDMA believes this practice should be maintained in the new standards FDA is developing. Distributors do not apply labeling to medicines. Therefore, we do not have the experience to answer this question.

b. What are the associated costs for the application, use, and maintenance of standardized numerical identifiers?

There is always a cost associated with increasing the safety and security of the supply chain, but we believe the benefits of enhanced product safety, increased distribution efficiencies and the ability to trace the product's transaction history outweigh the costs. Due to the fact that company implementations will differ significantly, it is difficult to project specific costs and potential benefits.

c. What are the associated costs or processes for updating the standards as needed?

Currently, standards are developed and maintained by GS1 Healthcare. For companies participating in GS1, there could be annual corporate membership and meeting registration fees set by GS1, individual travel expenses and other similar costs. Many GS1 Healthcare meetings, for instance, are held overseas, creating both travel time and costs. As a result, industry representation can be limited to those companies willing to contribute staff time and financial resources, which can create a disparity in participation across supply chain segments.

HDMA recommends that FDA specify the standards and the data elements within those standards that should be used in the United States for item identification and track and trace. HDMA also recommends establishing a process for evaluating the standards with industry on a periodic basis to update them, as necessary.

d. What are the benefits of using standardized numerical identifiers?

Multiple numerical identifiers will impose significant costs on companies downstream from the manufacturer, which will have to maintain multiple systems to read multiple, non-standard schemas. A single, standard identifier, with a single, standard data carrier, applied to individual units at the point of manufacture, ensures uniqueness of the identifier and limits cost and complexity (e.g., creating processes for each type of identifier, staff training for each, data reading and exchange) across the supply chain. The use of a single, interoperable standard also ensures that regulatory authorities can leverage common systems across the supply chain to review pedigree information and investigate violations.

4. Harmonization With Other Countries

a. What standards or unique identification systems do other countries have in place, currently under development, or planned for the future? If they are under development, please include a timeline for completion.

GS1 develops global standards, but they are implemented differently based on regional regulatory requirements. Countries have adopted GS1 standards such as GTIN (global trade item number), but encode country-specific numbers (i.e. NDC) within the GTIN. This is specifically provided for by the standards.

We recommend that FDA specify the standards and the data elements within those standards that should be used for item identification and for tracking and tracing prescription medicines in the U.S. supply chain.

b. Comment on any ‘‘lessons learned’’ from foreign experience with standardized numerical identifiers.

HDMA does not have lessons learned from foreign experience with standardized numerical identifiers. However, some foreign countries do use different “identifiers” that are similar to the NDC, but these numeric identifiers are not standardized across countries. Also, some foreign countries use their identifiers for different purposes than what Congress has mandated in the FDAAA .

B. Standards for Validation

There is significant confusion associated with the FDAAA references to "validation" of prescription drugs and the statute's applicability to establishing standardized numerical identifiers on prescription drugs. Foremost, distributors receive, hold and ship finished pharmaceutical products, and do not have any role in the "validation" of those drug products. HDMA is not aware of the use of the term "validation" in the context of product identification or tracking and tracing of prescription medicines, even though HDMA and its members have worked extensively with these issues for many years.

Confusion further arises because HDMA believes that the term "validation" is generally understood in the pharmaceutical industry as referring to documented evidence that a specific system, process or facility that is operated within established parameters can perform effectively and reproducibly to produce a result or outcome within predetermined specifications and quality attributes. *See, e.g.*, FDA Office of Regulatory Affairs Guide to Inspections, Glossary of Computerized System and Software Development Terminology, http://www.fda.gov/ora/inspect_ref/igs/gloss.html. Usually, processes and procedures are validated, not a product.

FDA, of course, already has some of the extensive standards that the FDAAA orders the agency to develop. The FDAAA instructs FDA to "develop standards and identify and validate effective technologies for the purpose of securing the drug supply chain against counterfeit, diverted, subpotent, substandard, adulterated, misbranded, or expired drugs" and "develop standards for the … validation … of prescription drugs." § 913(a)(b)(1), FDAAA, Food, Drug and Cosmetic Act, § 505D(a), 21 U.S.C. § 355e(a)(b)(1) Note. Standards for assuring the consistent safety, efficacy and potency of prescription drugs are set out in FDA's Good Manufacturing Practices (GMP) regulations, 21 C.F.R. Parts 210 and 211, and in the agency's numerous guidances and other policies. *See, e.g.*, FDA Guidance for Industry, CGMP Practice, http://www.fda.gov/cder/guidance/index.htm#CGMPS-Eff; Guidance for Industry International Conference on Harmonisation-Quality,

http://www.fda.gov/cder/guidance/index.htm#International%20Conference%20on%20Harmonisation-Quality.

Moreover, as FDA finalizes regulations and guidances concerning establishment of a single numerical identifier, as Congress envisions in the FDAAA, it will likely be necessary to describe standards for how manufacturers should validate (e.g., document) a procedure for assuring consistent production of prescription medicines with the mandated, standard numerical identifier. FDA would likely describe these new requirements for validating standardized numerical identifier processes in GMP regulations and drug manufacturing guidances. In regulation and guidance, FDA would be able to describe how a manufacturer should validate its systems for adding a standardized numerical identifier to a prescription medicine.

HDMA is very concerned with any extension of "validation" beyond its commonly understood and well-established regulatory meaning in the pharmaceutical industry. It is our understanding that "validation" of the "drug" itself would require physically examining medications to identify size, form, markings, color, etc. Disturbing a pharmaceutical's finished packaging configuration during product distribution in the supply chain violates sound distribution practices, and potentially comprises product integrity, exposing patient medications to greater risks of degradation, contamination, tampering and diversion.

Should, however, FDA interpret FDAAA to require "validation" of every prescription medicine beyond what already is done under existing regulations, HDMA believes such requirements should be limited in application to only those stakeholders who have a legitimate need to breach the manufacturer's packaging and inspect the medications inside (i.e. manufacturers and dispensers / administrators). Currently, each party in the supply chain has a role to play. The manufacturer ensures proper manufacture and packaging of the medication in accordance with the terms of its FDA approval to assure safety, potency, purity and efficacy. The distributor preserves the medication's FDA-approved packaging configuration, and moves the product effectively and efficiently, while

preserving product integrity. The pharmacy dispenses the medication appropriately to the patient, in accordance with the prescriber's orders.

Validating individual prescription medicines also would result in significant cost associated with product loss. Additionally, there would be significant increase in process cost to develop a system for performing "validation" of prescription medicines.

In sum, before undertaking any further changes to "validation" of prescription medicines, HDMA urges FDA to carefully examine the extent to which its existing requirements sufficiently secure the prescription medicine supply, and to whom those requirements do and should apply. Given the confusion and ambiguity in the FDAAA surrounding the term "validation," HDMA further urges FDA to provide an opportunity to review any definition or standard for "validation of prescription drugs" that arises from this request for comments, before it is adopted as final.

C. Standards for Track and Trace

HDMA understands the definition of track and trace to be the ability to locate an item in the supply chain (track) and the ability to verify the path it took to get to that location in the supply chain (trace).

1. Do standards currently exist for track and trace of products in the supply chain, generally?

Track-and-trace standards are under development by GS1, but they are not complete at this time. These global track-and-trace standards are being developed for use in many industries. The FDA should specify the specific standards and the specific data elements within those standards that should be used for tracking and tracing prescription medicines in the U.S. healthcare supply chain.

GS1 has developed a pedigree messaging standard that allows companies to transmit pedigree information to the next downstream trading partner, essentially allowing only for the "trace" part of track and trace. The GS1 pedigree

messaging standard is not a standard for track and trace.

a. If so, please describe and comment on their application and use.

Since track-and-trace standards have not yet been completed, we cannot comment on specific instances of application and use.

b. To what extent do these standards reflect stakeholder consensus?

These standards are being developed in the GS1 global and multi-industry environment. Stakeholders involved in the GS1 process have not yet completed work on the final standards. Please note that participation in this standards development process and consensus building may not be reflective of the total U.S. healthcare supply chain. Cost and time constraints have limited participation in these and other standards efforts of some U.S. healthcare supply chain stakeholders. The FDA should specify the specific standards and the specific data elements (as noted in section C.4) within those standards that should be used to track and trace prescription medicines in the U.S. healthcare supply chain.

c. Comment on whether any of these standards should be the standard adopted by FDA.

HDMA supports the standards development process within GS1, but believes it should include broader U.S. industry review and consensus to ensure the standards are applicable to the U.S. supply chain. If broad industry consensus is achieved, FDA should adopt these standards. For industry-wide adoption of these standards, consideration must be given, however, to removing any economic barriers to using the standards, such as royalties or memberships.

c. If yes, why? Compare this standard with other standards that exist.

HDMA is not aware of other track-and-trace “standards” that exist or are in development. There may be other proprietary protocols and procedures that are in use, but these generally are used in closed systems only.

e. If not, is there some aspect that could be changed to make it acceptable as the FDA standard?

f. Has this standard been adopted by other countries?

No, the standards are not complete.

g. If standards are under development or planned for the future, please include a timeline for completion.

HDMA is working with GS1 on their comments and we expect them to address projected timetables for standards development.

2. Do standards currently exist for track and trace of prescription drug products in the supply chain?

Track-and-trace standards are under development by GS1, but they are not complete at this time. These global track-and-trace standards are being developed for use in many industries. The FDA should specify the specific standards and the specific data elements within those standards that should be used to track and trace of prescription medicines in the U.S. healthcare supply chain.

GS1 has developed a pedigree messaging standard that allows companies to transmit pedigree information to the next downstream trading partner, essentially allowing only for the “trace” part of track and trace. The GS1 pedigree messaging standard is not a standard for track and trace.

a. If so, please describe and comment on their application and use.

Since track-and-trace standards have not yet been completed, we cannot comment on specific instances of application and use.

b. To what extent do these standards reflect stakeholders consensus?

These standards are being developed in the GS1 global and multi-industry environment. Stakeholders involved in the GS1 process have not yet completed work on the final standards. Consensus building and participation in this standards development process is not reflective of the total U.S. healthcare supply chain. Cost and time constraints have limited participation in these and other standards efforts of some U.S. healthcare supply chain stakeholders. The FDA should specify the specific standards and the specific data elements within

those standards that should be used to track and trace of prescription medicines in the U.S. supply chain.

c. Comment on whether any of these standards should be the standard adopted by FDA.

HDMA supports the standards development process within GS1, but believes it should include broader U.S. industry review and consensus. If broad industry consensus is achieved, FDA should adopt these standards. Consideration must be given, however, to removing any economic barriers to using the standards, such as royalties or annual memberships.

d. If yes, why? Compare this standard with other standards that exist.

HDMA is not aware of other track-and-trace "standards" that exist or are in development. There may be other proprietary protocols and procedures that are in use, but these generally are used in closed systems only.

e. If not, is there some aspect that could be changed to make it acceptable as the FDA standard?

f. Has this standard been adopted by other countries?

3. Are standards in development for track and trace of prescription drugs in the supply chain? If so, who is developing these standards and what is the timeline for completion?

HDMA is working with GS1 on the development of standards for the tracking and tracing of prescription medicines. They are currently in the requirements-gathering phase. GS1 is managing the process and is responsible for establishing and keeping to a timeline. Although HDMA supports the GS1 development process, there are defects in the process due to the limited number of participants and the fact that some segments of the healthcare supply chain may not be represented at all.

4. What are the elements, provisions, and particular considerations that should be included in a track and trace standard for prescription drugs? Please be specific in your response and include examples, where possible.

A track-and-trace standard should be based on a unique identification number incorporating the NDC and a serial number; incorporate standard, unique location identification (Global Location Number-GLN); start at the point of manufacture (where it enters the commercial supply chain) and end at the point of dispense or destruction; should record critical events (receiving and shipping at each location in the supply chain); and have query capabilities. The critical data elements are:

- Standard numerical identifier which includes NDC and serial number.
- Standard unique location identifier for location (ship to, sold to).
- Legend name.
- Container size.
- Invoice quantity.
- Dosage form and strength.
- Manufacturer (unique identifier).
- Unique transaction number that can be tied to invoice number.
- Transaction date.
- Lot number.
- Expiration.

HDMA believes the standard numerical identifier belongs on each individual item, using RFID as the carrier. All other information could be included in electronic track-and-trace standard transactions.

Provisions that need to be taken into account for track and trace are:

- Clear definition of supply chain participants:
  - Manufacturers
  - Distributors
  - Pharmacies
  - Doctors
  - Clinics
  - Reverse Distributors.
- Record retention policies.

- Standardized data exchange format.
- Clear definition of package size (lowest saleable unit to the point of dispense or administration).
- Data carrier with specific data format defined (i.e. RFID with NDC and serial number encoded).
- Reporting guidelines for exceptions are being developed by industry in GS1 Healthcare US.

5. Please comment on implementation of track and trace for prescription drugs in the U.S. supply chain, including, but not limited to, feasibility, costs, timeline, interoperability, information technology, and data storage.

It is difficult to specifically comment on the implementation of track and trace for prescription medicines because there is no comparable model in other industries. Each company's investment will vary, depending on their position in the healthcare supply chain, the systems they choose to deploy, the number of products that must be tracked and traced, etc. In order to be effective, however, all segments of the supply chain will need to make some level of investment in enhancing the safety and security of the system, on behalf of patients. HDMA believes that in addition to the safety benefits, track-and-trace systems also hold the most promise for increasing efficiencies, streamlining operations, enhancing value and eliminating waste, which may offset some of the costs of deployment. One standard for the country, rather than 50 potentially conflicting state requirements, will be more efficient and less costly. The development of end-to-end systems based on the unique identification and tracking of individual prescription drugs will achieve true, long-term safety benefits for all Americans. *Therefore, we believe that a national, electronic track-and-trace system based on item-level serialization that starts with the manufacturer holds the most promise for improving the security of the healthcare supply chain.*

The HDMA Healthcare Foundation's 2004 study, *Adopting EPC in Healthcare: Costs & Benefits*, suggests that systems integration costs for large distributors and manufacturers to install and implement an RFID system could be $10-$15 million per company. Manufacturers will also have ongoing costs associated with

applying data carriers at the item level, but the study predicted falling RFID tag costs as adoption increases.

The study also pointed out that while initial efforts to use RFID / EPC would focus on supply chain integrity, companies could expect to achieve annual benefits in the tens of millions of dollars. Benefits identified in the study include improved supply chain integrity, improved deduction and claim accuracy and greater warehouse and inventory efficiency. These costs are constantly decreasing and are difficult to estimate.

With respect to timelines for implementation, a prerequisite for the supply chain to track and trace product is to first have products serialized with machine-readable unique identifiers. Only then will the supply chain be able to read / scan products as they move through facilities to the ultimate prescriber or dispenser. Thus, track and trace is inexorably linked to progress on product serialization.

Once product is serialized, however, there should be a sufficient time allotted for distributors to adjust processes and facilitate track and trace in both the receiving and shipping functions of a distribution center. Given the millions of products received and shipped each day by distributors, this is a significant undertaking that would require a period of time to implement after products are serialized.

Moreover, additional time should be considered for implementation of track and trace at the dispenser/provider-level, given the vast (144,000+) number of sites where medicine is dispensed or administered. Similar to distributors, dispensers/providers would need to adjust receiving processes to accommodate track and trace. Consideration must be given to the scope of the intended implementation, recognizing that track and trace across the entire U.S. supply chain would take more time than adopting for a single state or a subset of products.

6. Discuss how the data generated from track and trace should be held, where it should be held, concerns related to data security, and means for access to ensure

interoperability for data sharing. What elements should be included in such a standard for data exchange, storage, and interoperability?

As long as the industry can leverage interoperable standards, individual companies can make their own choices as to how and where track-and-trace is held, based on their own level of sophistication and business policies. Point-to-point systems imply that data is held within each company and can be accessed by trading partners via query requests. A network registry, however, may offer more capabilities for meeting industry demands. Please reference the Center for Healthcare Supply Chain Research report, *Rules of Engagement: Phase II: The Blueprint for Data Management and Data Sharing*. Any standards developed for track and trace and data sharing should include security measures that prevent unauthorized sharing of supply chain data.

7. Comment on any ‘‘lessons learned’’ from foreign experience with track and trace.

HDMA is not aware of any comparable track-and-trace models in other industries.

D. Standards for Authentication

HDMA understands that authentication is the process of reading the standard numerical identifier on the package at the end customer or dispenser location to determine if the item was produced and distributed by the manufacturer in the supply chain. In other words, such a process allows the pharmacy to authenticate the product package directly with the manufacturer, and does not provide for tracking and tracing item-level chain of custody information across the supply chain. HDMA recognized that under PDMA, distributors still have documented chain of custody pedigree requirements, which can be met by the track-and-trace provisions. Therefore, it is assumed that authentication would be performed by manufacturers and pharmacies.

1. Do standards currently exist for authentication of products in the supply chain, generally?

There are proprietary authentication solutions in use, but HDMA is not aware of any common industry standards. Currently, the business requirements for authentication are under development at GS1 Healthcare and EPCglobal. After

the business requirements have been agreed upon, the standards development process will begin. Please refer to GS1 regarding timetables for standards development.

a. If so, please describe and comment on the application and use.

There have been some limited pilots of authentication using proprietary solutions in Europe and the United States. HDMA does not have access to details of these pilots, but we understand that European tests are intended to meet foreign requirements. The domestic tests do not help companies meet existing pedigree requirements.

b. To what extent do these standards reflect stakeholders consensus?

These standards are being developed by GS1. GS1 includes stakeholders from many industries, such as fast-moving consumer goods, and gathers requirements on a global basis. Stakeholders involved in the GS1 process have not yet completed work on the standards. Consensus building and participation in this standards development process is not reflective of the total U.S. healthcare supply chain, and is being directed by an organization based out of Belgium. Cost and time constraints have limited participation in these and other standards efforts of some U.S. healthcare supply chain stakeholders.

Additionally, package authentication is not required and does comply with existing pedigree requirements.

c. Comment on whether any of these standards should be the standard adopted by FDA.

Currently, there isn't a supply chain standard. We believe that a track-and-trace system based on item-level serialization that starts with the manufacturer holds the most promise for improving the security of the healthcare supply chain.

d. If yes, why? Compare this standard with other standards that exist.

e. If not, is there some aspect that could be changed to make it acceptable as the FDA standard?

f. Has this standard been adopted by other countries?

Authentication may be in use in other countries, but it is not based on a common standard. Countries have implemented proprietary authentication requirements for reimbursement and to deter fraud.

2. Do standards currently exist for authentication of prescription drug products in the supply chain?

HDMA is aware that there are proprietary solutions available; however, we do not know of common industry standards. Please refer to GS1 regarding timetables for standards development.

a. If so, please describe and comment on the application and use.

There have been some limited pilots of authentication in Europe and the United States. HDMA does not have access to details of these pilots.

b. To what extent do these standards reflect stakeholders consensus?

These standards are being developed in the GS1 global and multi-industry environment. Stakeholders involved in the GS1 process have not yet completed or agreed upon final standards. Consensus building and participation in this standards development process is not reflective of the total U.S. healthcare supply chain, and is being directed by an organization based out of Belgium. Cost and time constraints have limited participation in these and other standards efforts of some U.S. healthcare supply chain stakeholders. Additionally, package authentication is not required and does not comply with existing pedigree requirements.

c. Comment on whether any of these standards should be the numerical identifier standard adopted by FDA.

Authentication is a process that uses the numerical identifier, but authentication does not establish the identifier. Countries have implemented proprietary authentication requirements for reimbursement and to deter fraud. Although HDMA doesn't believe authentication standards should be adopted by FDA, if FDA chooses to adopt authentication standards, there could be limited benefit by implementing the standards at the pharmacy level.

d. If yes, why? Compare this standard with other standards that exist.

e. If not, is there some aspect that could be changed to make it acceptable as the FDA standard?

f. Has this standard been adopted by other countries?

3. Are standards in development for authentication of prescription drugs in the supply chain? If so, who is developing these standards and what is the timeline for completion?

There are proprietary solutions, but HDMA does not know of common industry standards. Currently, the business requirements are under development at GS1. HDMA recommends that FDA refer to GS1 for information concerning timetables for standards development.

4. What are the elements, provisions, and particular considerations that should be included in an authentication standard for prescription drugs? Please be as specific as possible and include examples, where possible.

HDMA does not believe that an authentication standard for prescription medicines should be developed by FDA. Work in this area could divert focus and resources from item-level serialization and track and trace.

5. Please comment on implementation of authentication for prescription drugs in the U.S. supply chain, including, but not limited to, feasibility, costs, timeline, interoperability, information technology, and data storage.

6. Comment on any ‘‘lessons learned’’ from foreign experience with authentication.

HDMA understands that the authentication models used in Europe are a) only in pilot stages and b) based on proprietary technologies.

E. Prioritization

Please comment on the priority for development and implementation of identification, validation, authentication, and tracking and tracing standards.

HDMA believes that an electronic track-and-trace system based on item-level serialization that starts with the manufacturer and ends at the point of dispense or destruction holds the most promise for improving the security of the healthcare supply chain. Therefore, we believe FDA's priorities should be as follows:

1 – identification
2 – tracking and tracing
n/a – validation
n/a – authentication

Since HDMA believes that item-level serialization and electronic track and trace hold the most promise to increase the security of the supply chain, we do not believe that FDA should adopt standards for validation or authentication, as we have described in previous sections within this response.

1. Should certain standards be developed and implemented before others?

A prerequisite for the supply chain to track and trace product is to first have products serialized with machine readable unique identifiers. Only then will the supply chain be able to read / scan products as they move through facilities to the ultimate prescriber or dispenser. Thus, track and trace is inexorably linked to progress on product serialization.

Once product is serialized, however, there should be a sufficient time allotted for distributors to adjust processes and facilitate track and trace in both the receiving and shipping functions of a distribution center. Given the millions of products received and shipped each day by distributors, this is a significant undertaking that would require a period of time to implement after products are serialized.

Moreover, additional time should be considered for implementation of track and trace at the dispenser/provider-level, given the vast (144,000+) number of sites where medicine is dispensed or administered. Similar to distributors, dispensers/providers would need to adjust receiving processes to accommodate track and trace. Consideration must be given to the scope of the intended implementation, recognizing that track and trace across the entire U.S. supply

chain would take more time than adopting for a single state or a subset of products.

2. Should certain standards be developed and implemented concurrently?