Testimony to US FDA Public Workshop Regarding the Determination of System Attributes for the Tracking and Tracing of Prescription Drugs

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PREFACE

Pharma Logic Solutions, LLC leverages extensive first-hand experience and lessons learned to provide guidance and consulting services to support traceability, serialization, e-Pedigree and supply chain collaboration to those involved in the manufacturing and distribution of prescription drugs. Pharma Logic Solutions differentiates itself in the way it helps companies utilize their existing systems with minimal changes to address traceability or e-Pedigree compliance. We are often contracted to develop strategies, user requirement specifications (URS), solution architectures, vendor selection and validation materials. We offer this testimony document to the US FDA to improve public safety through greater control of the distribution of prescription drugs.

During the course of our business we have been told that pharmaceutical companies are reluctant to employ solutions for serialization or traceability until specific guidance and definitions are provided by the FDA or governmental regulatory organizations. The concern is that if they invest in traceability now, to gain the benefits from traceability found in other industries, that future regulatory guidance may contradict their approach and result in additional investment and business disruption. Instead, many businesses wait to see what will be required. News that the FDA is considering guidance without a specific deadline further frustrates the situation.

With the approaching implementation of legislation from the State of California, that requires traceability, serialization and the transmission of electronic chain-of-custody documents (pedigree) by 2015, many businesses are faced with a decision to disrupt their business to implement a solution specific to the California law. They know that legislation from other states or future federal legislation may require additional traceability requirements, or may supersede or contradict the requirements by California.

We further note that traceability solutions that may be suitable for large pharmaceutical manufactures or wholesalers may be too costly for smaller organizations at the end of the supply chain, such as local drug stores or small independent hospitals and clinics. While it has been stated that this presents an opportunity for solution providers, we are concerned that given current economic challenges many smaller drug stores, hospitals or clinics may not be able to continue to offer prescription drugs if the cost to comply with new traceability requirements is too great.

The following document suggests a specific approach to tightly control the pharmaceutical supply chain, by leveraging proven techniques used in other industries, in a cost effective way. Pharma Logic Solutions hopes that the FDA will consider the cost, varying requirements at different stages in the drug supply chain, potential business disruption and time to implement a solution and will publish a roadmap with milestones as soon as possible.

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1 Introduction

Pharma Logic Solutions, LLC supports the FDA’s initiatives to formulate a national system to secure the custody of prescription drugs as they move through the supply chain. We welcome the opportunity to offer a straw man proposal\(^1\) for chain of custody control.

1.1 Purpose

This straw man proposal is intended to balance the needs of manufacturers, contracted service providers, wholesalers, distributors, healthcare providers and pharmacies in support of prescription drug traceability. The straw man proposal also seeks to address issues that arose during litigation\(^2\) over the PDMA in 2006, which enjoined the FDA from implementing 21 CFR § 203.50(a)\(^3\).

The purpose of this document is to offer a highly secure, cost effective solution to meet the goals expressed by the US FDA during the Public Workshop on the Determination of System Attributes for Tracking and Tracing of Prescription Drugs held in Washington, DC on February 15-16, 2011.

The stated goals of a track and trace system for prescription drugs (including biologics) included the following:

1. Preventing the introduction of counterfeit, diverted, subpotent, substandard, adulterated, misbranded, or expired drugs.
2. Facilitating the identification of counterfeit, diverted, subpotent, substandard, adulterated, misbranded, or expired drugs.
3. Providing accountability for the movement of drugs by supply chain participants.
4. Improving efficiency and effectiveness of drug recalls.

The document is structured to facilitate the development of user requirement specifications. The development of requirements is intended to foster industry input and the validation of future solutions.

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\(^1\) A “straw man proposal” is a brainstormed simple proposal intended to generate discussion of its pros or cons and to provoke the generation of new and better proposals. Often, a straw man document will be prepared by one or two people prior to kicking off a larger project. In this way, the team can jump start their discussions with a document that is likely to contain many, but not all the key aspects to be discussed.

\(^2\) Preliminary Injunction ordered 12/5/06 in RXUSA Wholesalers, Inc. v. HHS

\(^3\) 21 CFR § 203.50(a)(6), states that information regarding “each prior transaction involving the drug, starting with the manufacture” be included in the pedigree. The court order also enjoins FDA from implementing the language in 21 CFR § 203.50 that requires pedigrees to include lot and control numbers, dosage, container size, and number of containers.
1.2 Background

a) Many recent pharmaceutical serialization and traceability initiatives have been driven largely by emerging state regulatory requirements. In many traceability projects, this has led to solutions that are very limited and fail to provide benefits to the organization beyond merely meeting the immediate specific regulatory requirement.

b) Serialization alone does little to actually thwart counterfeiting. Counterfeiters can produce counterfeit products with authentic looking serial numbers, LOT codes and expiration dates. Counterfeiters can also produce product with randomly sequenced serial numbers, so the added complexity of randomly generated serial numbers alone also does not prevent counterfeiting. They can also produce products with properly encoded radio frequency identification (RFID) tags using encoding systems costing less than US$2000. In fact, counterfeit packaging quality is often as good as or better than the authentic product and encoding or complicated and covert markings do not prove authenticity.

c) Without tight control and authentication of each change-of-custody, criminals many inject authentic looking inefficacious or dangerous fakes, complete with serial numbers and LOT codes, into the supply chain. The complexity of the US drug supply chain also allow fakes to be sold into legitimate channels unless they can be tightly tracked from inception, through contract operations, repacking, distribution and to the point of dispensing, destruction or recall.

d) Combining a SNI with the use of electronic chain-of-custody management systems and by tracking the relationship of serialized contents to a serialized container, often referred to as aggregation or a child-to-parent relationship, can improve confidence in the authenticity of prescription drugs.

e) With pharmaceutical counterfeiting, tampering, theft and diversion said to be on the rise, many manufactures in the pharmaceutical industry are turning to techniques widely used in other industries to protect their brand. This is done at the risk that the techniques may not meet future state or federal drug tracking mandates. Moreover, absent a federal mandate or a consistent industry-wide technique for the control of custody, actual counterfeiting, tampering, theft or diversion may not be fully known or able to be fully measured or benchmarked.

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4 Katherine Eban, Dangerous Doses: How Counterfeiters Are Contaminating America’s Drug Supply (Houghton Mifflin Harcourt)
5 http://www.fda.gov/RegulatoryInformation/Guidances/ucm125505.htm
6 http://www.securingpharma.com/40/articles/815.php
g) Legislation in California\(^7\), which requires serialization, traceability and electronic chain of custody control (e-Pedigree) by 2015, has resulted in many prescription drug manufactures starting projects to encode products using the FDA’s SNI or GS1 standards. Likewise, many of these companies have also begun projects to enhance business systems to manage serialized goods. These projects may be leveraged if the chain of custody system proposed by the FDA is based on industry standards, such as those offered by GS1, and considers existing serialization systems, such as serial number event repositories.

h) In addition, a chain of custody security tracking system may only need to track minimal information about each item to achieve a secure exchange of custody. To reduce further delay, the FDA security tracking system may not need to address all supply chain collaboration needs but rather focus only on chain of custody. Further supply chain collaboration could be supported using existing electronic data interchange solutions such as EDI, HL7 and EPCIS.

i) Confusion over central versus distributed data systems may further delay the identification of a specific solution for industry. The concept of secure package tracking, which allows the originator and intended recipient to track the package as it moves through the delivery chain, have been perfected by companies such as Federal Express, UPS and the US Postal Service. These systems commonly use a highly available central database design. In most cases, information is replicated to multiple physical databases but appears to the users as a single data source. Access is available through multiple connections to the various physical databases and then synchronized through replication across the physical databases. As an example of successful highly available large scale tracking systems, consider when the last time you heard that FedEx or UPS tracking was not available. Other examples of highly available central databases include popular search engines such as Google, Bing, Yahoo or major banking systems.

j) If we consider prescription drug authentication initiatives in other areas of the world, we see the emergence or use of state controlled central databases used to authenticate prescription drugs for reimbursement. While driven by reimbursement, these systems do demonstrate that central, state controlled, databases are viable. The FDA’s goal of protecting the public from dangerous drugs is no less of a reason to implement traceability than reimbursement.

k) However, it should be considered that the emerging European *bookend* approach to tracking, where the manufacture and point of dispensing are the only supply chain points involved, may not prevent a counterfeit copy of an authentic drug from being the first of a specific serial number to be registered as dispensed. In this case, the counterfeit would be considered authentic and dispensed to the patient while the real drug would be considered fake because it was second to arrive at a pharmacy with the same serial number.

\(^7\) http://www.pharmacy.ca.gov/about/e_pedigree_laws.shtml
l) Also expressed as a concern during the February 2011 FDA workshop were issues involving data visibility and ownership of the data. By establishing a Federal Distribution License (FDL), the FDA can certify who can be involved in interstate commerce of prescription drugs. Included with the FDL can be security and access control information for the specific licensee. These access controls can then be used to identify those who have had or will have custody of a specific SNI encoded item. To avoid the misuse of supply chain and trade data, only those in the chain of custody should have access to the records for a specific SNI. There are many nonproprietary systems and techniques for establishing secure virtual private networks (VPN) that could be chosen by the FDA to secure access.

m) Existing electronic data interchange solutions such as EDI, HL7 and GS1’s electronic product code information services (EPCIS) do provide some degree of supply chain security by allowing recipients of goods to electronically query information from the originator of a shipment. Absent systems to reliably discover every custodian of a specific item, and absent a system to securely authenticate those transacting chain of custody information, we submit that these solutions are inadequate alone to maintain the degree of control required to ensure the security of the US prescription drug supply chain. These systems may be leveraged to accomplish the solution proposed in section 2 of this document or to provide expanded supply chain collaboration information.

n) Distributed decentralized systems, specifically for the control of the chain of custody, may add unnecessary complexity by requiring those seeking to manage custody to first identify where data are located, then retrieve the information from multiple data pools and assemble and organize the information for their needs. For optional enhanced supply chain collaboration a centralized chain of custody system may be augmented by distributed systems and data pools, such as GS1’s EPCIS and global data synchronization network (GDSN).

o) Transaction volume concerns were expressed during the February FDA workshop and have the potential to create delays in establishing guidance for traceability. If we assume the annual volume of US prescriptions is 4 billion, and we assume that the worst case would be that each prescription is a single package from the manufacture (and not a bulk container), and we assume that each single package is exchanged 20 times between manufacture and patient consumption, we would expect 219,179 transactions per day for tracking. We recognize that there will be spikes in transaction and that volume will vary by time of day or day of week. We further recognize that the actual packages will be less than the 4 billion prescriptions due to bulk packages dispensed into smaller quantities at the pharmacy. In 2008, FedEx reported that it delivered 3.6 million\textsuperscript{8} packages on average daily throughout the United States and package tracking for each step in the delivery chain was tracked from a central database. The capacity to manage several times the transactions discussed above is well within the capabilities of many databases.

\textsuperscript{8} http://online.barrons.com/article/PR-CO-20110218-907747.html
p) The management of a centralized chain of custody system by the FDA could be self-funded by those who use the system. Cost could be based on transaction volume, which will likely be less than the cost for each supply chain participant to develop and manage a separate e-Pedigree system. The development of the system, implementation and operation could be outsourced to a service provider. Service providers seeking to win a bid to provide the solution should have to demonstrate how they will meet the FDA requirements and present their expected transaction cost. To ensure the system leverages the latest technology, the FDA could limit the term and allow service providers to bid on the system every few years. As the solution provider changes, the connection information, such as server domain name, and communication standards would not need to change and the transition could have minimal impact of the supply chain participants.

q) With respect to an FDA central database, the FDA currently registers every person who owns or operates any establishment in any State engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs each year under Section 510(b) of Food Drug and Cosmetic Act (FD&C). Likewise, the FDA registers foreign entities under Section 510(i) of FD&C. A DUNS (Dunn and Bradstreet) number is required for each facility (not a single corporate number) and an optional FEI (FDA Establishment Identifier) may also be provided.

r) In some situations it is felt that the relatively low cost or special nature of some prescription drugs will not be of interest to a counterfeiter and those drugs may be excluded. Lessons learned from the more than 21 reported deaths associated with counterfeit heparin in 2008 have taught us that relatively low cost drugs are not only susceptible to adulteration but that the results can be deadly. Or consider the more than 100 people who died in 2006 after consuming cough syrup and toothpaste produced with diethylene glycol, a toxic chemical sometimes used in antifreeze, instead of glycerol. While these examples involve tainted components, they do demonstrate that counterfeiters do not ignore low cost drugs. The absence of tight controls over chain of custody complicates the recall process. The absence of even LOT level electronic tracking data increase the difficulty of isolating tainted product. A centralized chain of custody system would allow the distribution of any tainted prescription drug to be halted and an exact count of tainted product in pharmacies and healthcare facilities to be known. The on package encoding of LOT and expiration may further facilitate the identification of those at risk and may augment point of dispensing systems.

s) And finally, an FDA governed chain of custody management system could be used in the future to augment the FDA’s electronic health record (EHR) initiatives for patient prescription records or to identify other areas of public concern such as doctor shopping.

10 http://www.nytimes.com/2007/05/30/world/asia/30china.html
11 http://www.fda.gov/Safety/FDAsSentinelInitiative/ucm2007250.htm
2 Proposed Solution

2.1.1 For the purpose of this straw man proposal, we will refer to the system as the **serial encoded anti-counterfeiting logistics or FDA SEAL system**. This straw-man proposal is intended to generate discussion of its pros or cons and to provoke the generation of new and better proposals, leading to requirements and guidance from the FDA for the control of the chain-of-custody of prescription drugs. Our hope is that future federal legislation will both secure and facilitate the interstate trade of prescription drugs and improve patient safety and availability.

2.1.2 We propose that the system be self-funded and hosted by a service provider selected during a bid process. The criteria for selecting the service provider should be based on their ability to meet requirements, their service level commitment or agreement, security commitment and their proposed transaction fee. We further propose the term of the contract be three (3) years and the contract rebid based on updated requirements, lessons learned during the previous term and use of new technology.

2.1.3 The federal government and US tax payers should not be required to fund the system to manage the purity of prescription drugs traded in interstate commerce. By spreading the cost over those who use it, which will likely be less than separate systems maintained by each trading partner, and less complex than systems required to scan and assemble information from multiple data pools, the overall cost should be less to consumers.

2.1.4 We propose a high availability central database model, where no less than two physical data facilities, located in different regions of the United States, allow connection and store data. Data is to be automatically replicated between the facilities and failover routing systems used to automatically redirect connection traffic in the event of a failure.
2.1.5 We propose the FDA establish a Federal Distribution License (FDL) to certify who can be involved in interstate commerce of prescription drugs and to establish access credentials for each licensee to the FDA SEAL. To improve security and traceability, the holder of an FDL should have separate credentials for each physical access point used to connect with the FDA SEAL.

It should be noted that the FDA currently registers every person who owns or operates any establishment in any State engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs each year under Section 510(b) of Food Drug and Cosmetic Act (FD&C). Likewise, the FDA registers foreign entities under Section 510(i) of FD&C. A DUNS (Dunn and Bradstreet) number is required for each facility (not a single corporate number) and an optional FEI (FDA Establishment Identifier) may also be provided.

2.1.6 We propose that the FDA select, based on industry feedback, one or more secure virtual private networks (VPN) techniques to secure communications between the central system and FDL licensee facility.

2.1.7 When a FDL licensee accesses the system for the purpose of transacting change-of-custody information, the identification of the licensee will be automatically included in each record. This eliminates the potential for a licensee to spoof the system and create counterfeit records.

2.1.8 To avoid the misuse of supply chain and trade data, only those in the chain-of-custody, or those indicated as intended recipients should have access to the records for a specific SNI encoded item.

2.1.9 For the purpose of this document, a contractor is considered an extension of the manufacturer while the manufacturer retains liability for the prescription drug. If the contractor has an FDL, they may use it for accessing the FDA SEAL. If the contractor does not have an FDL and is acting as an agent of the manufacture, the manufacturer may establish the contractor connection information under their FDL. In doing so, the FDL licensee accepts liability for the contractor and is responsible for validating the contractor’s practices on their behalf.

2.1.10 We propose that information be communicated to and from the FDA SEAL using nonproprietary XML web services, transmitted within a secure virtual private network (VPN) between the FDA SEAL and registered FDL licensee network. We propose the exact message structure be defined during the expansion of this straw man proposal into functional requirements and strongly suggest the use of existing electronic product code information services (EPCIS) from GS1. We recognize that the current EPCIS standard will need to be expanded to accommodate the requirements proposed in this straw man document.
2.1.11 When a manufacture or their contractor agent has determined that a production LOT of prescription controlled drugs is available for distribution in interstate commerce, prior to the first shipment of the drug, they will submit the following information to a LOT Control (LC) Table in the FDA SEAL; (a) full NDC of saleable unit (including package configuration), (b) manufacturer’s LOT number, (c) expiration date, (d) total quantity of saleable units in the LOT, (e) date of manufacture, (f) location of manufacture.

The FDA may wish to also include a field in the LC table to include the IP address where additional product data may be found and a field for the method the data may be accessed. This allows for the use of systems such as the GS1 global data synchronization network (GDSN), HL7, EDI or XML, to provide additional data from the manufacture.

All those in the supply chain who handle a given SNI with the specific LOT number, should be allowed access to query the LC for LOT information.

2.1.12 While current practices by some manufacturers may allow for multiple different NDC and package configurations in the same LOT (same LOT number), we suggest that this practice be eliminated and a specific LOT number include only one saleable unit NDC and package configuration.

This table provides a single, national LOT control to cross reference a manufacturer’s LOT number. The purpose is to provide a central repository for LOT specific information and to facilitate recalls. Information on location and date of manufacture are included to facilitate recalls based on a facility. Total quantity is included to reconcile PASS records and related SNI to account for all items and prevent the insertion of counterfeit products containing the same manufacturer’s LOT number.

2.1.13 The LC will automatically record the FDL of the originator of the LC record and return a LOT Record ID (LRID), a unique number in the SEAL for the LOT information. The LRID avoids confusion when two or more identical LOT numbers from different manufacturers are recording in the LC.
2.1.14 When a manufacture or their contractor agent ships prescription drugs, they will produce a change-of-custody or Pharmaceutical Authentication Secure Shipping (PASS) record for each item in the packaging hierarchy in the FDA SEAL PASS table.

Each record will include; (a) SNI (or Globally Unique Trade Item Number and serial number, such as a GS1 GTIN and AI21) for the package, (b) SNI, or a Globally Unique Trade Item Number and serial number, or a Serialized Shipping Container Code (SSCC) for the package container, (c) LRID to link to manufacturer’s LOT information and (d) recipient FDL. The system will automatically record the FDL of the record originator and the date/time of the record creation.

For clarity, package hierarchy means each saleable unit and all parent containers up to and including the largest container being traded, including but not limited to saleable items, distribution packs or bundles, shipping cases, insulated containers and pallets. Items a and b above represent a serialized content to serialized container relationship or aggregation. If there is not a container, the entry for b would be blank or null.

2.1.15 Only the originator should be allowed to alter the recipient FDL if a change is required.

2.1.16 When a recipient receives prescription drugs, they will access the FDA SEAL via a secure VPN using their FDL credentials and certify the change-of-custody. The recipient’s FDL will grant them access to the PASS records of packages shipped to them, see 2.1.11. The recipient will append the record of each saleable unit and container with an indicator that the item was received. The system will automatically record the date and time of the transaction. This completes the change-of-custody.

To facilitate the process of confirming a shipment, trading partners may wish to use widely used electronic data interchange (EDI), such as serialized hierarchical advanced shipping notices (ASN), referred to as EDI 856 messages. Other optional techniques may include the use of emerging standards such as GS1 electronic product code information services (EPCIS) or HL7. These systems may be used to provide an advanced notice of serialized goods and allow recipient systems to prepare a pending PASS confirmation to be sent once goods are received and confirmed.

2.1.17 We recognize that some reviewers may express concerns over situations where the recipient FDL does not match the FDL entered by the originator. We submit that this should not be allowed in a controlled chain of custody. The originator should be the only entity allowed to alter the recipient FDL in the PASS record and should be allowed to alter the FDL if the shipping information changes after the PASS record is created.
2.1.18 We expect that some reviewers may feel the parent child aggregation may not be necessary. We support the California e-Pedigree legislation’s requirement for content-to-container serialization and submit that without this relationship the ability for a counterfeiter to inject products as they are in transit is considerably easier and that a single serial number can be copied and is inadequate for authenticating a package.

We further recognize that a counterfeiter could replicate content to container relationships, although the effort is considerably greater and more complex than replicating single serial numbers and the effort may greatly reduce the profitability, and by extension the likelihood, of counterfeiting prescription drugs.

2.1.19 We expect some reviewers to express concern over identifying the serial numbers of items within sealed containers and the practice of inference or inferring information. We submit that as items are removed from larger containers and exchanged through the controlled system described above, that direct observation will take place at least once at the end of the supply chain before distribution to a final recipient.

If containers were opened and the contents replaced with counterfeit product, the diverted legitimate product would have no way of reentering the supply chain and the container would eventually be opened and the counterfeit items would not have records in the FDA SEAL. We understand that a counterfeiter could replace serialized contents with identically serialized counterfeits, although the complexity would likely make it unlikely and limit counterfeiter’s profitability to a point where it would not be worth the effort.

We further submit that manufactures validate their practices and processes and that the process of ensuring that recorded information regarding the contents of a sealed container is substantially equivalent to other validated processes. An example of how validation is used is the practice of validating that the correct drug and dose is placed in an unlabeled bottle during packaging and that the correct label is placed on that bottle.

2.1.20 We expect some reviewers to express concern over transaction time to process the chain of custody information. We submit that any system would have a transaction burden and that the proposed solution manages each change of custody step separately, so only limited history and information is involved in the transaction. Moreover, we submit that the use of a single, central system may reduce the overall transaction time, as opposed to distributed systems where the source of each data pool must be identified, identity of the requestor confirmed at each data pool, records accessed, organized and assembled for interpretation.
2.1.21 We expect some reviewers to express concern over all those in the supply chain for a given SNI having access to all previous transactions. We submit that this access may be useful in diversion detection by the manufacturer or others in the supply chain. We further submit that this would allow a manufacturer to scan for SNI using their NDC designation and identify were items were not produced by them.

2.1.22 We expect there will be questions regarding how this system would be impacted by a national disaster, where it may be prudent to temporarily suspend the system to expedite shipments to the impacted area. We submit that a procedure will be required to allow those with goods, where there may be a gap in the chain of custody, to recertify the goods and restart the FDA SEAL process. This may include providing a mechanism for the FDA to authorize this action. We further submit that without this process, the integrity of the system would always be in question due to goods in circulation following a disaster.

The procedure for handling gaps in the PASS records and reentry into the system may also be useful in the event of a catastrophic failure of the FDA SEAL, where the requirement to transact chain of custody using the FDA SEAL may be temporarily suspended.

2.1.23 We expect some reviewers will express concerns over using only the SNI, especially if they wish to ship some items from a LOT outside the United States. These reviewers may wish to use, for example, a standard GS1 GTIN and AI21 serial number. We submit that the system should not be limited to only SNI and should support any globally unique trading number and serial number combination and that the PASS system should confirm that a number combination in 2.1.11a/b (above) has not been used previously.

We recognize that the FDA has published guidance on the use of the SNI and that if the FDA requires only the SNI that manufacturers would simply need to produce separate packaging LOT/batches for US versus non-US, a practice that many manufacturers do anyway.
2.1.24 For each change-of-custody through the prescription drug supply chain in the United States, the process described in 2.1.14 and 2.1.16 will be repeated. Only the last PASS recipient should be allowed to start the next PASS record for each package and its contents.

While the process of certifying each chain of custody is simplified for legitimate trading partners using a central data pool, this tightly controlled chain of custody exchange, coupled with tightly controlled access to the system through a single licensing authority (the FDA), is intended to greatly complicate the process for a counterfeiter to inject goods into the supply chain, regardless of how many times goods are bought and sold or the complexity of the trading system.

Moreover, diversion and unauthorized trade channels will no longer be able to reenter the legitimate supply chain, since both the originator and recipient must be in agreement for the change-of-custody and identity is managed by a 3rd party, in this example the FDA using the FDL and associated VPN credentials.

2.1.25 To facilitate the recall of questionable prescription drugs, we propose providing two (2) processes.

(a) First, a method for manufacturers or the FDA to indicate in the LRID that a LOT is recalled. The creation of each SNI PASS record should confirm that the LRID record is not “recalled” when a new chain of custody PASS record is initiated.

(b) Second, that recalls automatically distribute a notice of all affected SNI and package identifiers included in a recall. The notice should be sent to the designated responsible individual for the last FDL licensee of each recalled SNI. The notice should include a process for the responsible party to indicate receipt of the notice and that actions are being taken to prevent consumption or identify impacted consumers. For clarity, we assume that the recipient would receive one notice listing all SNI in their custody and not hundreds of separate notices for each SNI.

2.1.26 The system should support the practice of repackaging, where saleable units are opened and the contents of one or more saleable unit are comingled and repackaged into new containers, often small quantities or into kits of multiple serialized items.

For the purpose of this proposed chain of custody control system, we propose a final PASS record be created by the FDL licensee responsible for repackaging that will indicate “REPACKAGED” as the destination. We further suggest that the repackaged products be treated as newly manufactured products. A new LRID record will be required and a new PASS record for each repackaged product.
2.1.27 The special case of repackaging poses a challenge for recalls from the original bulk manufacture. We propose the inclusion of the LC to LC relationship (LLR) cross reference table in the FDA SEAL. This table would include the new LOT LRID and the LOT LRID of every repackaged product consumed in the repackaging. In many cases this may be a one-to-one relationship, but we can imagine situations where multiple original LOTs are consumed in one repackaging LOT, or vice versa. The repackager will be required to update the LLR before they can create the LC record for their new LOT LRID or subsequent PASS records.

The recall process in 2.1.21 should process recalls through the LLR table and should mark repacked LOT LRID records as recalled if any of the original recalled product was repackaged. It should also notify the responsible party for each FDL of the PASS records for the repackaged products.

2.1.28 As with repackaging, the practice of “kitting,” where one or more items with SNI may be combined with other items in a KIT to facilitate their use at the point of care, poses a special case. We propose that when a KIT is created with one or more SNI, that the KIT be given a globally unique trade item number, such as a GS1 GTIN, and a unique serial number for each KIT. A final PASS record will be created by the FDL licensee responsible for kitting for each component of the KIT that will indicate “KIT” as the destination. The new KIT will then be processed using the PASS transactions as described above.

We propose the FDL licensee responsible for the kitting be responsible to update the LLR with the LOT LRID numbers for each item with an SNI in the KIT and create a new LOT LRID record for the KITS.

The recall process for kitting could work the same as 2.1.23 (above).

2.1.29 The special situation for the final dispensing of the drug may be addressed by allowing the FDL licensee at the point of dispensing to create a final PASS record where the destination is “DISPENSED.”

We further suggest the inclusion of an optional dispensing cross reference (DCR) table to allow the recording of the SNI with a reference number that may be used by the dispensing entity to identify the recipient for purposes of recall. Only the FDL licensee recording the recipient identification would be able to cross reference it to an actual recipient name. This is intended to satisfy confidentiality and HIPAA concerns.
2.1.30 The special situation of destruction should be considered. As with other end of supply chain activities discussed above, the FDL licensee responsible to the destruction should create a final PASS record where “DISTROYED” is indicated in the recipient field.

An expired or damaged product would be returned to the manufacturer or their agent responsible for destruction using the PASS process and the manufacturer or agent would end the PASS process by recording “DESTROYED” in the recipient field once it reaches their facility.

We understand the common practice of contracting destruction, especially of expired or damaged goods, to contracted service providers. We submit that the responsibility of controlling the custody of the goods remains with the responsible FDL licensee and that the FDL licensee establishes a process for updating the FDA SEAL for destroyed goods with their contractors.

2.1.31 As with destroyed goods, returned or sampled goods should be accounted for in the FDA SEAL, and the FDL licensee retain responsibility to create final PASS records for each SNI indicating “RETURNED” or “SAMPLED” in the respective destination field.

2.1.32 The special situations of stolen or mishandled goods should be accounted for in the FDA SEAL. In the event items are reported stolen, the originator of the shipment should update the PASS records for each SNI with the destination as “STOLEN.” In doing so, further chain of custody exchanges would not be allowed since any FDL licensee receiving the goods would not be able to accept the goods in the FDA SEAL or to create new PASS records for subsequent shipments.

2.1.33 The FDA may wish to provide a web portal of mobile device application to allow consumers who receive prescription drugs with SNI, to enter the SNI and confirm that the item was marked as dispensed by a valid FDL licensee and that the chain of custody records are intact. This may help promote the FDA’s initiatives to protect patient safety and ensure the purity of prescription controlled products.

If such services are available, those dispensing prescription drugs may wish to provide the SNI of the bulk drug container on each container dispensed to a patient. This would allow them to promote their efforts to support the FDA and allow consumers to authenticate the prescription drugs they receive.
2.1.34 We recognize that some reviewers may be critical of recalls based on LOT and not isolating specific SNI. We submit that we have discussed the case of stolen goods, and nothing in the current design would prevent a PASS record with a destination of “STOLEN” to stop future trading of a specific item (such as a limited set of items on a stolen truck).

2.1.35 We recognize that some reviewers may advocate using only the GS1 EPCIS system and allowing supply chain partners to manage security relationships. We submit that this approach is inadequate to track goods back to the original manufacturer. An example is the case where a trading company is established by a counterfeiter who injects counterfeit goods with valid duplicate serial numbers into the supply chain by selling them under the pretense of being overage (product purchased in a quantity greater than the company could use). When the manufacture is queried they would have a record of the serial number. Another example would be a similar case where uplabeling is done, which was discussed in the book Dangerous Doses\textsuperscript{13}.

We support EPCIS, once evolved to accommodate the needs discussed above in this section of the document, as a messaging standard. We submit that only a 3\textsuperscript{rd} party, such as the FDA, should control access security, that a central database be used to simplify and facilitate the review of an items history, and controls established where only the entity distributing the item can control who the recipient is and only the registered recipient can mark the transaction as complete and start the next exchange.

\textsuperscript{13} Katherine Eban, Dangerous Doses: How Counterfeiters Are Contaminating America's Drug Supply (Houghton Mifflin Harcourt)
3 Meeting the FDA Objectives

We assume that for clarity, the reviewer has read sections 1.2, Background, and 2, proposed solution, before reviewing this section. The information below may seem out of context if the previous sections have not been reviewed.

3.1 Preventing Introduction

3.1.1 Preventing the introduction of counterfeit, diverted, subpotent, substandard, adulterated, misbranded, or expired drugs.

3.1.1.1 As we discussed in section 2.1.4, we propose a high availability central database model, referred to in the following writing as the FDA SEAL or tracking database, where no less than two physical data facilities, located in different regions of the United States, allow connection and house data. Data is to be automatically replicated between the facilities and failover routing systems used to automatically redirect connection traffic in the event of a failure.

3.1.1.2 We propose in 2.1.5 that the FDA establish a Federal Distribution License (FDL) to certify who can be involved in interstate commerce of prescription drugs and to establish access credentials for each licensee to the FDA tracking database. The holder of an FDL may have multiple credentials for each physical location used to connect with the FDA tracking database.

3.1.1.3 We propose in 2.1.6 that the FDA select, based on industry feedback, one or more secure virtual private networks (VPN) techniques.

3.1.1.4 As we discussed in section 2.1.7, we propose that when a FDL licensee accesses the system for the purpose of transacting change-of-custody information, the identification of the licensee be automatically included in each record. This eliminates the potential for a licensee to spoof the system and create counterfeit records.

3.1.1.5 We further suggest in 2.1.16 that when a recipient receives prescription drugs, they access the FDA tracking database using their FDL credentials and certify the change-of-custody. The recipient's FDL should only grant them access to the records of packages shipped to them. The recipient should then append the record of each saleable unit and container with an indicator that the item was received. The system should automatically record the date and time of the transaction.
3.1.2 Authorized supply chain participants.

3.1.2.1 As we discussed in section 2.1.5, we propose the FDA establish a Federal Distribution License (FDL) to certify who can be involved in interstate commerce of prescription drugs and to establish access credentials for each licensee to the tracking system. We recommend the holder of an FDL be allowed to have multiple credentials for each physical location used to connect with the tracking systems.

3.1.3 Reintroduction of dispensed serial numbers

3.1.3.1 As we discussed in section 2.1.28, we propose that at the time of dispensing, the FDL licensee dispensing the prescription drug create a final change-of-custody record where the destination is indicated as “DISPENSED.” We further suggest the inclusion of an option dispensing cross reference (DCR) table to allow the recording of the SNI with a reference number that may be used by the dispensing entity to identify the recipient for purposes of recall.

3.1.3.2 Once the destination of the change of custody record is filled with the term “DISPENSED,” no further change-of-custody records would be allowed because FDL record field of the last change of custody would not include a FDL and therefore new PASS records could not be started.

3.2 Identification

3.2.1 Facilitating the identification of counterfeit, diverted, subpotent, substandard, adulterated, misbranded, or expired drugs.

3.2.1.1 As we discussed in section 2, we propose for each change-of-custody, the process described in 2.1.11 and 2.1.12 will be repeated. Only the last FDL licensee should be allowed to start the next change-of-custody record for each package and its contents.

3.2.1.2 This tightly controlled chain of custody exchange, coupled with tightly controlled access to the system by only FDL licensees and only a single point of data storage is intended to greatly complicate the process for a counterfeiter to inject goods into the supply chain, regardless of how many times goods are bought and sold or the complexity of the trading system. Moreover, diversion and unauthorized trade channels will no longer be able to reenter the legitimate supply chain, since both the originator and recipient must be in agreement for the change-of-custody and identity is managed by a 3rd party, the FDA using the FDL and associated VPN credentials.
3.2.1.3 The special situation of destruction was discussed in 2.1.30. As with other end of supply chain activities discussed above, the FDL licensee responsible for the destruction should create a final change-of-custody record where “DESTROYED” is indicated in the recipient field.

3.2.1.4 Like destroyed goods, in section 2.1.31 returned or sampled goods were discussed. The FDL licensee should retain responsibility to create final change-of-custody records for each SNI indicating “RETURNED” or “SAMPLED” in the respective destination field.

3.2.1.5 The special situations of stolen or mishandled goods was discussed in 2.1.34 and should be accounted for in the FDA tracking database. In the event items are reported stolen, the originator of the shipment should update the change-of-custody records for each SNI with the destination as “STOLEN.” In doing so, further chain of custody exchanges would not be allowed since any FDL licensee receiving the goods would not be able to accept the goods in the FDA tracking database or to create new change-of-custody records for subsequent shipments.

3.3 Accountability

3.3.1 Providing accountability for the movement of drugs by supply chain participants.

3.3.2 Initiation from manufacturer

3.3.2.1 As we discussed in section 2.1.11, we propose that when a manufacture or their contractor agent has determined that a production LOT of prescription controlled drugs is available for distribution, prior to the first shipment of the drug, we suggest they submit the following information to a LOT Control (LC) Table in the tracking system; (a) full NDC of saleable unit (including package configuration), (b) LOT number, (c) expiration date, (d) total quantity of saleable units in the LOT, (e) date of manufacture, (f) location of manufacture.

The LC could automatically record the FDL of the originator of the LC record and return a LOT Record ID (LRID), a unique number for the LOT information.

3.3.2.2 As discussed in 2.1.14, when a shipment takes place, we suggest the originator produce a change-of-custody (PASS) record for each item in the packaging hierarchy in the tracking system and the recipient certify receipt. This ensures that each exchange in custody is tightly controlled and that the originator and recipient of each shipment agree to the transaction and that their identity is controlled from a central 3rd party authority (the FDA).
3.3.3 Trading and change of custody

3.3.3.1 As we discussed in section 2, we propose that for each change-of-custody, the process described in 2.1.11 and 2.1.12 be repeated. We further suggest that only the last FDL licensee in the chain of custody should be allowed to start the next change-of-custody record for each package and its contents.

3.3.3.2 This tightly controlled chain of custody exchange, coupled with tightly controlled access to the system by only FDL licensees and with only a single point of data storage is intended to greatly complicate the process for a counterfeiter to inject goods into the supply chain, regardless of how many times goods are bought and sold or the complexity of the trading system. Moreover, diversion and unauthorized trade channels will no longer be able to reenter the legitimate supply chain, since both the originator and recipient must be in agreement for the change-of-custody and identity is managed by a 3rd party, the FDA using the FDL and associated VPN credentials.

3.3.4 Contracted operations

3.3.4.1 As we discussed in section 2.1.9, we suggest a contractor be considered an extension of the manufacturer while the manufacturer retains liability for the prescription drug. If the contractor has an FDL, they may be allowed to use it for accessing the tracking systems. If the contractor does not have an FDL and is acting as an agent of the manufacture, the manufacture may establish the contractor connection information under their FDL. In doing so, the FDL licensee accepts liability for the contractor and is responsible for validating the contractor’s practices on their behalf.

3.3.4.2 We further suggest in 2.1.5 that the FDA establish a Federal Distribution License (FDL) to certify who can be involved in interstate commerce of prescription drugs and to establish access credentials for each licensee to the FDA tracking database. The holder of an FDL may have multiple credentials for each access point used to connect with the FDA tracking database.

3.3.4.3 We recommend in 2.1.6 that the FDA select, based on industry feedback, one or more secure virtual private networks (VPN) techniques.
3.3.5 Repackaging

3.3.5.1 We discuss in 2.1.26 that the system should support the practice of repackaging, where saleable units are opened and the contents of one or more saleable unit are comingled and repackaged into new containers, often small quantities.

3.3.5.2 For the purpose of the chain of a custody control system, we propose a final change-of-custody record be created by the FDL licensee responsible for repackaging that will indicate “REPACKAGED” as the destination.

3.3.5.3 We further suggest that the repackaged products be treated as newly manufactured products and a system, as described in section 2.1.27 of this document, be used to cross reference the original bulk SNI with the new repackaged SNIs.

3.3.5.4 The special case of repackaging poses a challenge for recalls from the original bulk manufacture. As described in section 2, we propose the use of a special LOT to LOT relationship cross reference table in the tracking system.

3.3.5.5 This table could include the new LOT and the LOT code of every repackaged product consumed in the repackaging.

3.3.5.6 A recall of the original LOT could then process recalls through the LOT to LOT relationship cross reference table and could mark repacked LOT records as “RECALLED” if any of the original recalled product was repackaged. It should also notify the responsible party for each FDL of the change-of-custody records for the repackaged products, as described above in section 2.

3.3.5.7 As with repackaging, the practice of kitting, where one or more items with SNI may be combined with other items in a KIT to facilitate their use at the point of care, poses a special case and is discussed in 2.1.28.

We propose that when a KIT is created with one or more SNI, that the KIT be given a globally unique trade item number, such as a GS1 GTIN, and a unique serial number for each KIT. A final change-of-custody record could be created by the FDL licensee responsible for kitting that will indicate “KIT” as the destination.

We propose the FDL licensee responsible for the kitting be responsible to update the LOT to LOT relationship cross reference table with the LOT numbers for each item with an SNI in the KIT and create a new LOT record for the KITS.

The recall process for kitting could work the same as 3.3.5.4 (above).
3.3.6 Dispensing

3.3.6.1 In section 2.1.29, we describe how the special situation for dispensing may be addressed by allowing the FDL licensee at the point of dispensing to create a final change-of-custody record where the destination is indicated as “DISPENSED.”

3.3.6.2 We further suggest in 2.1.29 that the inclusion of an option dispensing cross reference (DCR) table to allow the recording of the SNI with a reference number that may be used by the dispensing entity to identify the recipient for purposes of recall.

3.3.7 Consumer access

3.3.7.1 As discussed in section 2.1.33, the FDA may wish to provide a web portal of mobile device application to allow consumers who receive prescription drugs with SNI, to enter the SNI and confirm that the item was marked as dispensed by a valid FDL licensee and that the chain of custody records are intact. This may help promote the FDA’s initiatives to protect patient safety and ensure the purity of prescription controlled products.

3.3.7.2 If such services are available, those dispensing prescription drugs may wish to provide the SNI of the container bulk drugs were dispensed from. This would allow them to promote their efforts to support the FDA and allow consumers to authenticate the prescription drugs they receive.

3.3.8 Expired products

3.3.8.1 As described in 2.1.31, expired returned or goods should be accounted for in the FDA tracking database, and the FDL licensee retain responsibility to create final change-of-custody records for each SNI indicating “RETURNED.”

By including expiration date in the LOT control (LC) table, as described in 2.1.11, recipients could electronically check the expiration date of products as they are shipped or received.

Optionally, manufacturer’s may encode the expiration date in the data carrier, such as a barcode, to facilitate the check for expiration each time an item is scanned. The inclusion of a LOT number in the data carrier may likewise help in facilitating the detection of recalled drugs during each scan.
3.4 Recalls

3.4.1 Improving efficiency and effectiveness of drug recalls.

3.4.1.1 As described in section 2.1.25, to facilitate the recall of questionable prescription drugs, we propose providing two (2) processes.

(a) First, a method for manufacturers or the FDA to indicate in the system (the LRID) that a LOT is recalled. The creation of each SNI change-of-custody record should confirm that the system (or LRID) record is not recalled.

(b) Second, that recalls automatically distribute a notice of all affected SNI and package identifiers included in a recall. The notice should be sent to the designated responsible individual for the last FDL licensee of each recalled SNI. The notice should include a process for the responsible party to indicate receipt of the notice and that actions are being taken to prevent consumption or identify impacted consumers. For clarity, we assume that the recipient would receive one notice listing all SNI in their custody and not hundreds of separate notices for each SNI.

3.4.1.2 We recognize that some reviewers may be critical of recalls based on LOT and not isolating specific SNI. We submit that we have discussed the case of stolen goods in section 2.1.34 of this document, and nothing in the proposed design in section 2 would prevent the production of individual change-of-custody records with a destination of “STOLEN” to stop future trading of the item.
3.5 Capture

3.5.1 Capability to capturing the unique identification of a product and the status of the product.

3.5.1.1 As we proposed in section 2, each exchange of goods in the supply chain would involve a two-step process, where an authorized party will create records for each SNI and the recipient will confirm the receipt of the SNI.

3.5.1.2 We recommend that manufacturers adopt the use of widely used encoding symbologies to facilitate the capture and recording of item tracking information.

3.5.1.3 We further recommend the use of symbologies such as those defined by GS1, to encode their goods with either the FDA SNI or a globally unique trade item number and unique item level serial number, such as GS1 GTIN with GS1 AI21 serial number.

3.5.1.4 We recommend that all tracking information, such as the SNI, LOT and expiration date be printed in 10 point sans serif type or larger and that all encoded information in data carriers (barcodes, RFID) be reproduced in human readable form in 10 point or greater sans serif font.

3.6 Interoperability

3.6.1 Ensure interoperability to enable supply chain participants to securely capture, store, and exchange track-and-trace data accurately and efficiently.

3.6.1.1 We recommend that information be communicated to and from the FDA tracking database using nonproprietary XML web services, transmitted within a secure VPN between the FDA tracking database and the registered FDL licensee network. The exact message structure may be defined during the expansion of this straw man proposal into functional requirements.

3.6.1.2 The FDA may wish to also include a field in the LOT table of the tracking database to include the internet protocol (IP) address where additional product data may be found and a field for the method the data may be accessed. This allows for the use of systems such as the GS1 global data synchronization network (GDSN), HL7, EDI or XML, to provide additional data from the manufacture.
3.6.2 How can interoperability be achieved between systems used by all supply chain participants?

3.6.2.1 We recommend that information be communicated to and from the FDA tracking database using nonproprietary XML web services, transmitted within a secure VPN between the FDA tracking database and the registered FDL licensee’s network.

3.6.2.2 We recommend that the FDA tracking system allow for the use of GS1 electronic product code information services (EPCIS) formatted messages for recording change-of-custody (PASS) once EPCIS standards are updated to accommodate the information described in section 2.

3.6.2.3 The exact message structure may be defined during the development of functional requirements.

3.6.3 How can data exchange (data format, data interpretation) be standardized?

3.6.3.1 We suggest that when a manufacture or their contractor agent has determined that a production LOT of prescription controlled drugs is available for distribution, prior to the first shipment of the drug, they submit the following information to a LOT Control Table in the FDA tracking database; (a) full NDC of saleable unit (including package configuration), (b) their LOT number, (c) expiration date, (d) total quantity of saleable units in the LOT, (e) date of manufacture, (f) location of manufacture.

3.6.3.2 The FDA may wish to also include a field in the LOT table to include the IP address where additional product data may be found and a field for the method the data may be accessed. This allows for the use of systems such as the GS1 global data synchronization network (GDSN), HL7, EDI or XML, to provide additional data from the manufacture.

3.6.3.3 We suggest that all those in the supply chain, for a given SNI, should be allowed access to query the tracking system for the chain of custody information about the specific item.

3.6.3.4 While current practices by some manufacturers may allow for multiple different NDC and package configurations in the same LOT, we suggest that this practice be eliminated and a specific LOT number include only one saleable unit NDC and package configuration.
3.6.3.5 Likewise, we suggest that when a manufacture or their contractor agent ships prescription drugs, they produce a change-of-custody record for each item in the packaging hierarchy in the FDA tracking database change-of-custody table.

Each record will include; (a) SNI (or Globally Unique Trade Item Number and serial number, such as a GS1 GTIN and AI21) for the package, (b) SNI (or Globally Unique Trade Item Number and serial number) for the package container, (c) LRID and (d) recipient FDL. The system will automatically record the FDL of the record originator and the date/time of the record creation.

3.6.3.6 And finally, we suggest that when a recipient receives prescription drugs, they will access the FDA tracking database using their FDA registered credentials (referred to as FDL licensee in section 2) and certify the change-of-custody. The recipient’s credentials will grant them access to the records of packages shipped to them, see 2.1.11d. The recipient will append the record of each saleable unit and container with an indicator that the record was received. The system will automatically record the date and time of the transaction. This completes the change-of-custody.

3.6.4 What other aspects should be standardized to achieve interoperability?

3.6.4.1 Other than the definition provided in section 2 of this document, we do not recommend any additional interoperability information.
3.7 Authentication

3.7.1 Authenticate the unique identifier (standardized numerical identifier or SNI1) and entire distribution history of each product.

3.7.1.1 As suggested in section 2, we recommend the manufacture initiate the SNI custody record and link each SNI custody record to a record of LOT information.

3.7.1.2 The process suggested includes a two-step process for each change-of-custody. Only FDA licensed trading partners should be allowed to access the tracking database and process change-of-custody.

3.7.1.3 The identity of the originator could be added to each record to help prevent falsifying records.

3.7.1.4 A recipient should only be allowed to access and mark the record of an SNI record as received if they are recorded as the intended recipient by the originator. We suggest that only the originator be allowed to adjust the record for the intended recipient should they wish to alter the shipping information.

3.7.1.5 Only those who are the originators or recipients of a specific SNI should have access to the history.

3.7.2 How can authentication of the package SNI be achieved?

3.7.2.1 As described in section 2, the two-step controlled process for change of custody ensures only FDA licensed entities are participating in the transaction.

3.7.2.2 The use of a single repository for change-of-custody information and tight access controls ensures that only authentic trading partners participate in a change-of-custody transaction.

3.7.2.3 Both the originator and the recipient must agree to the exchange and the originator should be the only entity to define the recipient.

3.7.2.4 As further described in section 2, several provisions are defined for potential end of distribution that will prevent the injection of counterfeit goods into the process.
3.7.3 How can each supply chain participant that handled the package be verified as a legitimate participant?

3.7.3.1 As described in section 2.1.14 and 2.1.16, the two-step controlled process for change of custody ensures only FDA licensed entities are participating in the transaction.

3.7.3.2 We suggest in section 2.1.14 that when a manufacture or their contractor agent ships prescription drugs, they produce a change-of-custody record for each item in the packaging hierarchy in the FDA tracking database change-of-custody table.

3.7.3.3 Each record will include; (a) SNI for the package, (b) SNI for the package container, (c) LOT and (d) recipient FDL. The system will automatically record the FDL of the record originator and the date/time of the record creation.

3.7.3.4 We discuss in 2.1.16 that when a recipient receives prescription drugs, they will access the FDA SEAL using their FDL credentials and certify the change-of-custody. The recipient’s FDL will grant them access to the records of packages shipped to them. The recipient may append the record of each saleable unit and container with an indicator that the record was received. The system will automatically record the date and time of the transaction. This completes the change-of-custody.

3.7.3.5 The use of a single repository for change-of-custody information and tight access controls ensures that only authentic trading partners participate in a change-of-custody transaction.

3.7.3.6 Both the originator and the recipient must agree to the exchange and the originator should be the only entity to define the recipient.
3.8 Pedigree

3.8.1 Ability to create an electronic pedigree at any point during the movement of the product through the supply chain.

3.8.1.1 As we suggested above, only authenticated participants in the chain of custody for a specific SNI should have access to the history of the specific item.

3.8.1.2 Because we advocate the use of a single data repository in section 2.1.4, a complete set of change of custody records could be assembled into a pedigree or complete chain of custody document.

3.8.1.3 Exchanges should be certified by a 3rd party, such as the FDA or their contracted service provider (as suggested in section 2.1.5) to enhance security.

3.8.1.4 The use of a central database simplifies identifying all participants in the chain of custody and avoids complexities associated with distributed systems, where the list of participants must be obtained, identities confirmed, multiple sources of data queried, data assembled and interpreted.

3.8.1.5 The use of a central system allow for manufacturers and wholesalers to obtain pedigree for items they have distributed and to use the information to detect trade channel abnormalities, diversion or counterfeiter’s misrepresentation of their goods. The potential for 2-way pedigree provides additional value over the California legislation’s 1-way e-Pedigree document model.
3.8.2 Contractors

3.8.2.1 As suggested above in section 2.1.9, a contractor may be considered an extension of the manufacturer while the manufacturer retains liability for the prescription drug. If the contractor has an FDL, they may use it for accessing the FDA SEAL.

3.8.2.2 If the contractor does not have an FDL and is acting as an agent of the manufacture, the manufacture may establish the contractor connection information under their FDL. In doing so, the FDL licensee accepts liability for the contractor and is responsible for validating the contractor’s practices on their behalf.

3.8.2.3 The same steps as in section 3.7.3 could be applied to contractors under these circumstances.

3.8.3 Dispensing

3.8.3.1 As discussed in section 2.1.29, the special situation for dispensing may be addressed by allowing the FDL licensee at the point of dispensing to create a final change-of-custody record where the destination is indicated as “DISPENSED.”

3.8.3.2 We further suggest the inclusion of an option dispensing cross reference (DCR) table to allow the recording of the SNI with a reference number that may be used by the dispensing entity to identify the recipient for purposes of recall.

3.8.3.3 As discussed in section 2.1.30, similar to dispensing, the special situation of destruction should be considered. As with other end of supply chain activities discussed above, the FDL licensee responsible to the destruction should create a final change-of-custody record where “DISTROYED” is indicated in the recipient field.

3.8.3.4 We understand the common practice of contracting destruction, especially of expired or damaged goods, to contracted service providers. We submit that the responsibility of controlling the custody of the goods remains with the responsible FDL licensee and that the licensee establishes a process for updating the FDA tracking database for destroyed goods with their contractors.

3.8.3.5 Other special situations for consideration may be stolen or mishandled goods should be accounted for in the FDA tracking database. In the event items are reported stolen, the originator of the shipment should update the change-of-custody records for each SNI with the destination as “STOLEN.” In doing so, further chain of custody exchanges would not be allowed since any FDL licensee receiving the goods would not be able to accept the goods in the FDA tracking database or to create new change-of-custody records for subsequent shipments.
3.9 Access to data

3.9.1 Enable appropriate access to track-and-trace data necessary to achieve system goals.

3.9.1.1 As we suggested above in 2.1.8, only authenticated participants in the chain of custody for a specific SNI should have access to the history of the specific item.

3.9.1.2 Because we advocate the use of a single data repository in section 2.1.4, a complete set of change of custody records could be assembled into a pedigree or complete chain of custody document.

3.9.1.3 The use of a central database simplifies identifying all participants in the chain of custody and avoids complexities associated with distributed systems, where the list of participants must be obtained, identities confirmed, multiple sources of data queried, data assembled and interpreted.

3.9.1.4 Because a 3rd party, such as the FDA or their contracted service provider as suggested in section 2.1.5, authenticates access based on established credentials and security techniques, the exchanges could be certified.

3.9.2 What type of data should each supply chain participant capture?

3.9.2.1 As described in 2.1.11, when a manufacture or their contractor agent has determined that a production LOT of prescription controlled drugs is available for distribution in interstate commerce, prior to the first shipment of the drug, they will submit the following information to a LOT Control (LC) Table in the FDA tracking database; (a) full NDC of saleable unit (including package configuration), (b) LOT number, (c) expiration date, (d) total quantity of saleable units in the LOT, (e) date of manufacture, (f) location of manufacture.

3.9.2.2 The LOT database could automatically record the FDL of the originator of the LOT record and return a unique number for the LOT information.

3.9.2.3 As described in 2.1.14, when a manufacture or their contractor agent ships prescription drugs, they will produce a change-of-custody record for each item in the packaging hierarchy in the FDA SEAL PASS table.

Each record will include; (a) SNI (or Globally Unique Trade Item Number and serial number, such as a GS1 GTIN and AI21) for the package, (b) SNI, or Globally Unique Trade Item Number and serial number, or GS1 serialized shipping container code (SSCC) for the package container, (c) LRID and (d) recipient FDL. The system will automatically record the FDL of the record originator and the date/time of the record creation.
3.9.3 How should data be captured and stored (e.g., centralized or decentralized system)?

3.9.3.1 In section 2.1.4, we propose a high availability central database model, where no less than two physical data facilities, located in different regions of the United States, allow connection and house data. Data is to be automatically replicated between the facilities and failover routing systems used to automatically redirect connection traffic in the event of a failure.

3.9.3.2 We further propose that the system be self-funded and hosted by a service provider selected during a bid process. The criteria for selecting the service provider should be based on their ability to meet requirements, their service level commitment or agreement, security commitment and the transaction fee.

3.9.3.3 We also propose the term of the contract be three (3) years and the contract rebid based on updated requirements, lessons learned during the previous term and use of new technology. The federal government and US tax payers should not be required to fund the system to manage the purity of prescription drugs traded in interstate commerce.

3.9.4 How can data be accurately, consistently, efficiently, and securely exchanged?

3.9.4.1 We recommend the FDA establish a Federal Distribution License (FDL) to certify who can be involved in interstate commerce of prescription drugs and to establish access credentials for each licensee to the FDA tracking system.

3.9.4.2 The holder of an FDL may have multiple credentials for each physical access point used to connect with the FDA tracking database.

3.9.4.3 We encourage the FDA to select, based on industry feedback, one or more secure virtual private networks (VPN) techniques.

3.9.4.4 When a FDL licensee accesses the system for the purpose of transacting change-of-custody information, the identification of the licensee could be automatically included in each record. This eliminates the potential for a licensee to spoof the system and create counterfeit records.

3.9.4.5 We recommend that information be communicated to and from the FDA tracking database using nonproprietary XML web services, transmitted within a secure VPN between the FDA tracking database and the registered FDL licensee’s network. We believe GS1 EPCIS could be extended to support these transactions.

3.9.4.6 The exact message structure may be defined during the development of functional requirements.
3.9.5 Who will have access to the data?

3.9.5.1 As discussed in section 2.1.24 above, to avoid the misuse of supply chain and trade data, we suggest that only those in the chain-of-custody, or those indicated as intended recipients should have access to the records for a specific SNI.

3.9.6 How will contractors access data on behalf of the responsible party?

3.9.6.1 As discussed in 2.1.9 above, we suggest that a contractor be considered an extension of the manufacturer while the manufacturer retains liability for the prescription drug. If the contractor has an FDL, they may use it for accessing the FDA SEAL.

3.9.6.2 Also discussed in 2.1.9, if the contractor does not have an FDL and is acting as an agent of the manufacture, the manufacture may establish the contractor connection information under their FDL. In doing so, the FDL

3.9.7 What happens when drugs are repackaged?

3.9.7.1 As discussed in 2.1.26 above, the system should support the practice of repackaging, where saleable units are opened and the contents of one or more saleable unit are comingled and repackaged into new containers, often small quantities. We propose a final change-of-custody record be created by the FDL licensee responsible for repackaging that will indicate “REPACKAGED” as the destination. We also discuss the similar case of kitting in 2.1.28.

3.9.7.2 As discussed in section 2.1.26, we further suggest that the repackaged products be treated as newly manufactured products. A new LOT record should be required and a new change-of-custody record for each repackaged product produced.

3.9.7.3 The special case of repackaging poses a challenge for recalls from the original bulk manufacture. We propose the inclusion of the LOT to LOT relationship (LLR) cross reference table in the FDA tracking database. This table would include the new LOT and the LOT of every repackaged product consumed in the repackaging. In many cases this may be a one-to-one relationship, but we can imagine situations where multiple original LOTs are consumed in one repackaging LOT, or vice versa.

3.9.7.4 The recall process outlined in section 2.1.21 could process recalls through the LLR table and could mark repacked LOT LRID records as recalled if any of the original recalled product was repackaged. It should also notify the responsible party for each FDL of the change-of-custody records for the repackaged products.
3.9.7.5 As with repackaging, the practice of kitting discussed in 2.1.28, where one or more items with SNI may be combined with other items in a KIT to facilitate their use at the point of care, poses a special case. We propose that when a KIT is created with one or more SNI, that the KIT be given a globally unique trade item number, such as a GS1 GTIN, and a unique serial number for each KIT. A final PASS record will be created by the FDL licensee responsible for kitting that will indicate “KIT” as the destination.

We propose the FDL licensee responsible for the kitting be responsible to update the LLR with the LOT numbers for each item with an SNI in the KIT and create a new LOT record for the KITS.

The recall process for kitting could work the same as described in section 2.1.23.

3.10 Data Security

3.10.1 Ensure security of data and systems from falsification, malicious attacks, and breaches.

3.10.1.1 As discussed in 2.1.5 above, we propose the FDA establish a Federal Distribution License (FDL) to certify who can be involved in interstate commerce of prescription drugs and to establish access credentials for each licensee to the FDA tracking system.

3.10.1.2 The holder of an FDL may have multiple credentials for each access point used to connect with the FDA tracking database.

3.10.1.3 We encourage the FDA to select, based on industry feedback, one or more secure virtual private networks (VPN) techniques.

3.10.1.4 When a FDL licensee accesses the system for the purpose of transacting change-of-custody information, the identification of the licensee could be automatically included in each record. This eliminates the potential for a licensee to spoof the system and create counterfeit records.

3.10.1.5 To avoid the misuse of supply chain and trade data, we recommend that only those in the chain-of-custody, or those indicated as intended recipients should have access to the records for a specific SNI.

3.10.1.6 For the purpose of this recommendation, we suggest in section 2.1.9 that a contractor be considered an extension of the manufacturer while the manufacturer retains liability for the prescription drug. If the contractor has an FDL, they may use it for accessing the FDA SEAL. If the contractor does not have an FDL and is acting as an agent of the manufacture, the manufacture may establish the contractor connection information under their FDL.
3.11 Maintaining confidentiality

3.11.1 Ensure confidential commercial information is protected.

3.11.1.1 As discussed in section 2.1.24 above, to avoid the misuse of supply chain and trade data, we suggest that only those in the chain-of-custody, or those indicated as intended recipients should have access to the records for a specific SNI.

3.11.1.2 As we suggested above, only authenticated participants in the chain of custody for a specific SNI should have access to the history of the specific item.

3.11.1.3 Because a 3rd party, such as the FDA or their contracted service provider as suggested in section 2, authenticates access based on established credentials and security techniques, the exchanges could be maintained confidential and protected.

3.12 Privacy

3.12.1 Ensure applicable patient privacy is maintained.

3.12.1.1 We do not recommend patient data be maintained in the FDA tracking system.

3.12.1.2 We suggest that the link between the SNI and specific recipient be maintained by the entity responsible for dispensing the prescription drug.

3.13 Disasters

3.13.1 Reentry of goods following a national disaster.

3.13.1.1 As discussed in 2.1.22, we suggest that the FDA tracking system support provisions for national disasters, where it may be prudent to temporarily suspend the system to expedite shipments to the impacted area. We suggest that a procedure be developed to allow those with goods, where there may be a gap in the chain of custody, to recertify the goods and restart the FDA tracking process. This may include providing a mechanism for the FDA to authorize this action.

3.13.1.2 We further submit that without this process, the integrity of the system would always be in question due to goods in circulation following a disaster.
3.13.2 A catastrophic failure of the system.

3.13.2.1 As discussed in 2.1.22, the procedure for handling gaps in the change-of-custody records and reentry into the system following disasters may also be useful in the event of a catastrophic failure of the FDA SEAL, where the requirement to transact chain of custody using the FDA SEAL may be temporarily suspended.

3.14 Support for GS1 standards

Pharma Logic Solutions would like to add its voice to those at the workshop who endorsed the GS1 standards. GS1 is a not-for-profit standard setting organization whose standards are accepted throughout the pharmaceutical supply chain, and are designed to be applied internationally. Among GS1’s standards are those for bar codes, location identification (i.e., the Global Location Number or GLN), product identification (Global Trade Item Number or GTIN), Radio Frequency Identification (RFID) and for implementing serialization requirements.

Based on Pharma Logic Solutions’ experience participating in GS1’s standard-setting activities, we believe that GS1 standards can be compatible with a potential pharmaceutical supply chain track and trace system; however, further refinement is needed to ensure absolute data consistency. Pharma Logic Solutions believes that GS1 still needs to provide more specificity for the number of characters and formatting to be used in the NDC portion of the SNI as well as the serial number portion. Further clarification and specificity is also needed regarding the use and standardization of the GLN in order to identify individual trading partners registered with the FDA.

We further support GS1 electronic product code information services (EPCIS) as a messaging standard, once they are evolved to accommodate the needs discussed above in section 2 of the document. We do however submit that only a 3rd party, such as the FDA, should control access security, that a central database be used to simplify and facilitate the review of a SNI encoded item’s history, and controls established where only the entity distributing the item can control who the recipient is and only the registered recipient can mark the transaction as complete and start the next exchange.
4 Appendix

4.1 Definitions, Acronyms, and Abbreviations:

Aggregation: is the process of recording the serial number of a container with the serial numbers of its contents, often referred to as parent/child relationship or serialized container to content relationship.

Application identifiers (AI): GS1 coding uses a series of Application Identifiers to include additional data such as best before dates, batch numbers, quantities, weights and many other attributes needed by the user.

AS2: Used in EDI. AS2 (Applicability Statement 2) is a specification about how to transport data securely and reliably over the Internet. Security is achieved by using digital certificates and encryption. The AS2 protocol is based on HTTP and SMIME

Authentication involves verifying that an SNI is a valid number for the package with which it is associated. It also involves verifying that the package was sold, purchased, traded, delivered, handled, stored, brokered by, or otherwise transferred from legitimate supply chain participants, and confirming that there are no discrepancies in the distribution history.

Bundle: a group of items held together, usually by shrink-wrap.

Case: a container or carton of items or shrink-wrapped bundles or boxes of items.

Counterfeiting: A counterfeit is an imitation, usually one that is made with the intent of fraudulently passing it off as genuine. Counterfeit products are often produced with the intent to take advantage of the established worth of the imitated product. The word counterfeit frequently describes both the forgeries of currency and documents, as well as the imitations of clothing, software, pharmaceuticals, jeans, watches, electronics, and company logos and brands. In the case of goods it results in patent infringement or trademark infringement.

Contract Packager: a company employed to package goods into containers and label the products. Contract packagers are also responsible for traceability and the collection of serialized container to content relationships.

Data management provides standardized mechanisms that supply chain participants use to capture, store, protect, and utilize track-and-trace data to facilitate authentication and interoperability. These mechanisms may include information for ensuring compliance of and accountability for established processes, as well as corrective action if these processes are not followed.

Datamatrix: a two-dimensional matrix barcode consisting of black and white "cells" or modules arranged in either a square or rectangular pattern. The information to be encoded can be text or raw data.
EFPIA: see European Federation of Pharmaceutical Industries and Associations

Electronic Product Code Information Services (EPCIS): EPC Information Services (EPCIS) is an EPCglobal standard designed to enable EPC-related data sharing within and across enterprises. This data sharing is aimed at enabling participants in the EPCglobal Network to obtain a common view of the disposition of EPC-bearing objects within a business context. More at www.epcglobalinc.org

Enterprise systems: Business software systems used by the entire company.

EPCglobal: EPCglobal is leading the development of industry-driven standards for the Electronic Product Code™ (EPC) to support the use of Radio Frequency Identification (RFID) in today’s fast-moving, information rich, trading networks.

EPCIS: see Electronic Product Code Information Services

e-Pedigree: an electronic document, typically in XML format, containing the history of custody. An e-pedigree (also epedigree) standard has been promulgated by GS1 and its EPCglobal division.

European Federation of Pharmaceutical Industries and Associations (EFPIA): European Federation of Pharmaceutical Industries and Associations (EFPIA) is a Brussels-based trade union founded in 1978 representing the research-based pharmaceutical industry operating in Europe. Through its direct membership of 31 national associations and 44 leading pharmaceutical companies, EFPIA is the voice on the EU scene of 2,200 companies committed to researching, developing and bringing new medical treatments.

Expiry: date of expiration or the last day the item should be used.

Event Repository (ER): a computer system designed to store serial number information, events relating to serialized products.

FDA SEAL: See SEAL

FDL: Federal Distribution License, a newly required certification that an entity involved in the interstate commerce of prescription drugs is authorized by the FDA and is further used to maintain access control records to the FDA SEAL.

Food and Drug Administration Amendments Act (FDAAA): On September 27, 2007, President George W. Bush signed the Food and Drug Administration Amendments Act of 2007 into law. It reviewed, expanded, and reaffirmed several existing pieces of legislation regulating the FDA. These changes will allow the FDA access to much-needed resources that will enable the agency to better protect American consumers by allowing more comprehensive reviews of potential new drugs and devices.

Global Trade Item Number: see GTIN
GS1: GS1 (www.gs1.com) is a leading global organization dedicated to the design and implementation of global standards and solutions to improve the efficiency and visibility of supply and demand chains globally and across sectors. The GS1 system of standards is the most widely used supply chain standards system in the world.

GTIN (Global Trade Item Number): is an identifier for trade items developed by GS1 (comprising the former EAN International and Uniform Code Council)[citation needed]. Such identifiers are used to look up product information in a database (often by inputting the number through a bar code scanner pointed at an actual product) which may belong to a retailer, manufacturer, collector, researcher, or other entity. The uniqueness and universality of the identifier is useful in establishing which product in one database corresponds to which product in another database, especially across organizational boundaries.

HDMA (Healthcare Distribution Management Association): is the national association representing primary, full-service healthcare distributors. HDMA member companies deliver more than nine million prescription medicines and healthcare products to more than 165,000 settings including chain and community pharmacies, hospitals, nursing homes, physician offices and clinics in every state and territory.

IMPACT (International Medical Products Anti-Counterfeiting Taskforce): WHO has responded to the challenge by creating a global coalition of stakeholders called IMPACT (International Medical Products Anti-Counterfeiting Taskforce). The taskforce, created in 2006, has been active in forging international collaboration to seek global solutions to this global challenge and in raising awareness of the dangers of counterfeit medical products.

Inference: the technique of assuming the serial numbers of a sealed container based on previous observation and not directly reading each serial number. Inference is accomplished using data systems or documents (see pedigree) and is controlled through validated procedures.

Interoperability establishes compatible data and process standards to enable system participants to have the capability of sharing data by integrating into the same system.

Kitting: the practice of combining one or more item with an SNI into a KIT for convenience at the point of care.

Label: the USA Federal Food, Drug and Cosmetic Act in Section 201(k) defines "label" as a: "display of written, printed, or graphic matter upon the immediate container of any article..."

LC: LOT Control, a unique number used to link a manufacture’s LOT, the NDC and the manufacture identity together for use in the FDA SEAL.

LLC: LC to LC relationship (LLR) cross reference table in the FDA SEAL to link the LOT identifier of goods in repacked or kitted product.

LRID: LOT Record ID, a unique number for the LOT information.
LOT: A group of products, usually associated by a manufacturing or packaging operation. Also see Batch.

PASS, a change-of-custody record in the FDA SEAL.

Pedigree: a document containing the history of custody. The pedigree document may be exchanged as paper or in electronic form.

Prescription Drug Marketing Act (PDMA): The Prescription Drug Marketing Act (PDMA) of 1987 (P.L. 100-293, 102 Stat. 95) is a law of the United States federal government. It establishes legal safeguards for prescription drug distribution to ensure safe and effective pharmaceuticals. It's designed to discourage the sale of counterfeit, adulterated, misbranded, subpotent, and expired prescription drugs. It was passed in response to the development of a wholesale sub-market (known as the "diversion market") for prescription drugs.

Repackaging: the practice of consuming bulk prescription drugs into new packaging, often small packages.

RFID (Radio Frequency Identification): Radio-frequency identification (RFID) is the use of an object (typically referred to as an RFID tag) applied to or incorporated into a product, animal, or person for the purpose of identification and tracking using radio waves. Some tags can be read from several meters away and beyond the line of sight of the reader.

SEAL: Serial Encoded Anti-counterfeiting Logistic system, used to manage and control the change of custody of prescription drugs.

Serial Number: a unique identifier to distinguish one item from a similar item.

Serialized Global Trading Item Number (sGTIN): a global trade item number and serial number encoded into an RFID tag. Not used when discussing barcodes.


For most prescription drug packages, the SNI is described as a serialized National Drug Code (sNDC) which is composed of the National Drug Code that corresponds to the specific drug product (including the package configuration), combined with a unique serial number of up to 20 characters. NDC numbers are not currently used for certain biological products approved under Section 351 of the Public Health Service Act, such as blood and blood components and certain minimally manipulated human cells, tissues, and cellular and tissue-based products (HCT/Ps). The SNI for these products should be the unique identification number created for each package under other recognized standards, such as ISBT 128.

3PL (Third Party Logistics): a contracted company responsible for the distribution of finished goods on behalf of the company, such as UPS.
4.2 About the author

The preceding document was prepared by Mr. William (Bill) Fletcher. His background spans over 29 years in pharmaceutical, medical devices, enterprise software and healthcare systems.

Mr. Fletcher is available to leverage the experience and lessons learned that are demonstrated in the preceding document to help organizations prepare for California, European EFPIA, various international and potential US Federal traceability and e-Pedigree requirements. At the time of this writing he has completed traceability, serialization and e-Pedigree projects for 9 leading pharmaceutical and biologics companies, including strategies, user requirements, functional designs, vendor selection, pilot implementation and validation.

As Managing Partner of Pharma Logic Solutions, LLC, Mr. Fletcher leverages his deep subject matter and project management experience to help solve complex business problems. His experience in life sciences spans from packaging/labeling automation and inspection systems, serialization, barcoding, radio frequency identification (RFID), distribution systems, e-Pedigree/RxASN and supply chain track and trace to drug discovery and R&D, clinical trials, brand marketing and physician education.

He has managed teams of technology professionals and projects throughout the pharmaceutical lifecycle. Mr. Fletcher has spoken and published numerous times on issues within the pharmaceutical industry. He is a member of several industry advisory groups and as such has had an impact on guiding the way organizations navigate the issues driving business strategy. In addition, Mr. Fletcher has experience in regulatory compliance, validation of operating systems (computer and manufacturing) in accordance with CFR Title 21 Part 11, GxP, GAMP versions 4 and 5, contracting strategies and systems, business intelligence and knowledge systems (including portals), and integration of software applications into enterprise business systems such as SAP.

Mr. Fletcher is currently focused on pharmaceutical serialization, track and trace and anti-counterfeiting. He has developed serialization and e-Pedigree strategy, requirements, vendor selection and project planning for multiple companies. In a prior role, Mr. Fletcher was director of development for a leading provider of packaging execution systems (PES). In that role Mr. Fletcher led development teams for multiple serialization and RFID projects, including for a highly publicized serialization, RFID and e-Pedigree deployment for multiple top 10 global pharma companies.

Mr. Fletcher is a long standing member of the Project Management Institute (PMI), a member of GS1 US Healthcare and has received various industry certifications, including SAP Auto identification infrastructure (Aii) for managing encoding and auto-identification systems.
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