Evaluation of the Impact of 2D Barcodes on Vaccine Secondary Packaging

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Executive Summary

Ongoing regulatory efforts to bolster drug distribution security have promoted an enhanced focus on ways to leverage data carriers to improve how pharmaceutical product information is stored, managed, and used. It has become clear that linear barcode technology has inherent functionality limitations. To transcend these limitations, leading industry stakeholders have begun to evaluate alternative data carrier technologies. This investigation has been evident within the vaccine industry and has manifested in the passing of Title II of the Drug Quality and Security Act (DQSA)—also referred to as the Drug Supply Chain Security Act (DSCSA).

Effective industry pilot programs involving the use of 2D barcoding, coupled with various concerns (e.g., costs and prohibitions) related to the use of Radio Frequency Identification (RFID) technology for biologics, have led to vaccine industry opinions that 2D barcodes will become the industry data carrier standard for secondary packaging. Secondary packaging is the saleable unit, most often the carton, of the vaccine. The DSCSA confirmed the use of 2D barcodes as the standard data carrier for secondary packaging through its requirement that vaccine manufacturers apply 2D barcodes to secondary packaging no later than November 2017.

Using 2D barcodes on vaccine secondary packaging can provide several benefits, including increased data carrier storage capacity and scalability; improved data capture accuracy and efficiency; enhanced product verification; and compliance with regulatory requirements. The predominant value derived from 2D barcodes on vaccine secondary packaging will be improved inventory management capabilities across the entire vaccine industry, which includes manufacturers, distributors, health care providers, and public health systems.

An industry move toward 2D barcodes on secondary packaging for vaccines will not be without challenges. Supply chain stakeholders will incur varying degrees of implementation costs both to produce and scan 2D barcodes, and to store the additional information from 2D barcodes. Companies will also need to make several process changes to accommodate the new technology. Current serialization, track and trace and e-pedigree regulation timelines further complicate these challenges. Traceability, sometimes referred to as Track and Trace, is the concept of maintaining visibility to a product as it travels throughout the supply chain in order to enhance patient safety. The goal is to confirm that products are legitimately in the supply chain, handled properly, and are safe to dispense. Traceability is enhanced by an electronic document, or e-pedigree, as the product moves through the supply chain. An e-pedigree provides the history of transactions regarding a product.

Despite the challenges, it is apparent that in the coming years, adoption of 2D barcodes within the United States vaccine industry is imminent as stakeholders work toward meeting regulatory requirements. Likewise, similar regulatory requirements abroad will likely drive 2D barcode adoption as the global standard.

Based on interviews with vaccine supply chain stakeholders and other publicly available information, we can state the following key findings regarding the adoption of 2D barcodes on vaccine secondary packaging:

- 2D barcodes will become the industry standard for vaccine secondary packaging as vaccine manufacturers work to meet the DSCSA requirement to apply 2D barcodes to secondary packaging. Improved inventory management resulting from adopting 2D barcodes on vaccine secondary packaging will be the main benefit to downstream supply chain members

- The current lack of understanding, use, and coordination of data standards and operational capabilities across the vaccine supply chain complicates adoption of 2D barcodes. DSCSA regulations will push the use of 2D barcodes to the forefront of the industry to accommodate the guidance to encode products with standard numerical identifiers

Going forward, industry stakeholders will do well to align their expectations for 2D barcodes together while identifying and remediating known and emerging adoption challenges. Collaborative supply chain activities should include improving education and outreach regarding 2D barcodes across many stakeholders. Additionally, conducting end-to-end pilots of 2D barcodes on secondary packaging, and engaging systems vendors to determine compatibility with inventory management and EMR systems may likely speed adoption.

1 Background and Overview

1.1 Report Background

During investigation for the original publication (May 2013) of this report, there was uncertainty whether a state-based or federalized mandate would drive serialization requirements. The signing into law of Title II of the Drug Quality and Security Act (DQSA) also referred to as the Drug Supply Chain Security Act (DSCSA) in November of 2013 removed this uncertainty. This updated report reflects changes required by DSCSA requirements and incorporates new information identified since its original publication.

Serialization of U.S. pharmaceutical products at the saleable unit is a key catalyst for the adoption of 2D barcodes. The increased data capacity and smaller footprint 2D barcodes offer relative to linear barcodes makes 2D barcodes a logical solution for encoding the unique identifiers needed to meet pharmaceutical serialization requirements.

Ongoing regulatory efforts to bolster drug distribution security have promoted an enhanced focus on ways to leverage data carriers to improve how pharmaceutical product information is stored, managed, and used. It has become clear that linear barcode technology has inherent functionality limitations. To transcend these limitations, leading industry stakeholders have begun to evaluate alternative data carrier technologies. This investigation has been evident within the vaccine industry and has manifested in the passing of DSCSA that confirmed the use of 2D barcodes as the standard data carrier for secondary packaging through its requirement that vaccine manufacturers apply 2D barcodes to secondary packaging no later than November 2017.

Effective industry pilot programs involving the use of 2D barcoding, coupled with various concerns (e.g., costs and prohibitions) related to the use of Radio Frequency Identification (RFID) technology for biologics, have led to vaccine industry opinions that 2D barcodes will become the industry data carrier standard for secondary packaging. Secondary packaging is the saleable unit, most often the carton, of the vaccine. These pilot programs have demonstrated a variety of benefits of 2D barcoding over traditional industry standard data carrying technologies for primary and secondary packaging. Such benefits include increased data carrier storage capacity and scalability; improved data capture accuracy and efficiency; enhanced product verification; and proactive, early compliance with forthcoming regulatory requirements. While all of these benefits are attractive to the industry, the predominant value derived from 2D barcodes on vaccine secondary packaging will be improved inventory management capabilities across the entire vaccine industry (including manufacturers, distributors, and health care providers).

An industry move toward 2D barcodes on secondary packaging for vaccines would not be without challenges. The issues are diverse and complex, and run the gamut of the regulatory and legislative landscape, touching many primary and secondary players in the vaccine supply chain and process. Additionally, the technology options available have benefits and disadvantages, which complicate clear decision-making. The details and nuances of a wider background and understanding of the current state of technology and 2D barcoding adoption provide important context to the debate between the status quo and emergent data carrier

technologies. For a more detailed overview of the vaccine industry and regulatory and legislative landscape surrounding 2D barcoding, please refer to the Appendices of this report.

In 2011, the Centers for Disease Control and Prevention (CDC) commissioned a two-dimensional (2D) vaccine barcoding pilot project to evaluate the impact and benefits to provider administration workflow, as well as data quality and completeness, when 2D barcodes were placed on primary packaging of vaccine products. The U.S. Food and Drug Administration (FDA) define primary packaging as the "packaging component that is or may be in direct contact with the dosage form."[1] This is the definition used for the pilot study. The 2D vaccine barcode pilot project specifically seeks to understand the opportunities that 2D barcodes offer to improve quality, accuracy, and completeness of vaccine administration data and its flow to the provider's Electronic Medical Records (EMR) and Immunization Information Systems (IIS).

1.2 Overview

This report serves as an extension of the 2D vaccine barcoding pilot and is intended to provide an evaluation of the impacts of 2D barcodes on vaccine *secondary* packaging. Secondary packaging is defined by the FDA and within this report as the "packaging component that is not and will not be in direct contact with the dosage form."[2] Understanding these impacts is important, as secondary packaging represents the lowest category of saleable-level packaging for vaccine products. Changes to secondary packaging have the potential to impact inventory management and data tracking throughout the vaccine supply chain. Secondary packaging will also be instrumental for tracking products as pharmaceutical track-and-trace regulations come into effect in the coming years.

This report describes the impact that the application and use of 2D barcodes on vaccine secondary packaging has on vaccine manufacturers, distributors, and providers. After discussing the specific benefits and challenges for these stakeholders, the report then outlines key findings and next steps for 2D barcode adoption.

Beyond the scope of this report, we include a broad discussion of the regulatory and legislative landscape; an overview of currently available 2D data carrier technologies; and an overview of the vaccine supply chain in the first three Appendices to this document. This report more narrowly focuses on an assessment of the potential impact of adopting 2D barcoding technology on vaccine secondary packaging.

1.3 Evaluation Approach

To conduct this evaluation, the team performed more than 20-targeted interviews with individuals who represent a cross section of vaccine supply chain roles or functions. Between October 2012 and January 2013, these interviews were conducted with leaders within the industry to gain their insights and perspectives on the impact and benefits of 2D barcoding on secondary packaging. Many of the interviews were held in person and some were held over the phone. The interviews included input from the following stakeholder groups:

- **Vaccines for Children (VFC) program** – The VFC program is a federally funded program that provides vaccines at no cost to children who might not otherwise be vaccinated because of inability to pay. Representatives of the VFC program, a large

[1] U.S. Department of Health and Human Services. "Container Closure Systems for Packaging Human Drugs and Biologics." U.S. Food and Drug Administration, May 1999. Web. <http://www.fda.gov/downloads/Drugs/Guidances/ucm070551.pdf>.
[2] U.S. Department of Health and Human Services. "Container Closure Systems for Packaging Human Drugs and Biologics." U.S. Food and Drug Administration, May 1999. Web. <http://www.fda.gov/downloads/Drugs/Guidances/ucm070551.pdf>.

purchaser of vaccines, were interviewed in order to learn how the transition to 2D barcodes on secondary packaging might affect the program's vaccine ordering and supply solution, VTrckS, and other components of the program's processes. Interviewees (1)

- **Vaccine Manufacturers** – Manufacturers are key stakeholders since they will be affixing or imprinting specific data carriers onto secondary packaging for the vaccine products they produce. Interviewees (6)

- **Distributors of Vaccine Products** – Distributors play a crucial role in the vaccine supply chain, transporting drugs from manufacturers to providers. Since distributors both receive and distribute product, they are directly impacted by any potential changes to product packaging. Interviewees (9)

- **Hospital Groups** – Hospital groups serve as aggregators, tying networks of hospitals and doctors together under umbrella organizations. We interviewed representatives of hospital groups to learn how the transition to 2D barcodes on secondary packaging might affect their networks. Interviewees (2)

- **Providers** – Providers are the hospitals, doctors, or organizations who actually administer vaccines to patients. We selected public health departments and leading U.S. pharmacies for interviews to assess the impact the transition to 2D barcodes on secondary packaging may likely have on their operations. Interviewees (2)

- **Industry Associations** – Industry associations are organizations founded and funded by businesses or individuals that operate in specific industries to share thought leadership and leading practices, and to promote industry goals. We interviewed representatives from provider industry associations to obtain an understanding of their members' perspectives related to 2D barcoding on secondary packaging. Interviewees (3)

The aggregated information from the interviews provides an understanding of the benefits and challenges anticipated by each stakeholder group. To help maintain participant confidentiality, the information presented in this report is referenced broadly and not attributed to responses from individuals or stakeholders.

The team also used industry publications, articles, and state and federal regulations and guidance to inform this report. Sources are cited throughout the report and collected in the bibliography section of the Appendices.

2 Supply Chain Impacts

This section provides an analysis of the supply chain impacts, or the benefits and challenges of 2D barcode adoption for manufacturers, distributors, and providers. Benefits accrue in areas of information storage capability and scalability; data accuracy and data use efficiency; product verification; and, regulatory compliance. The benefits across the stakeholders are contained in Table 1 at the end of Section 2.1.

Challenges are categorized by implementation costs, procedural changes, and regulatory concerns. Like the benefits, challenges affect each stakeholder contingency differently, across manufacturers, distributors, and providers. The challenges across the stakeholders are contained in Table 2 at the end of Section 2.2.

2.1 Benefits of 2D Barcodes on Vaccine Secondary Packaging

The placement of 2D barcodes on vaccine secondary packaging represents a substantial opportunity to enhance overall inventory management, and is an important step toward increasing the security of the vaccine supply chain via the use of serialization. Adoption of 2D barcode technology provides stand-alone, serialization-specific, and e-pedigree enabling benefits. Among the many potential impacts, 2D barcodes on secondary packaging can enable operational efficiencies, reduce human error, improve inventory and recall management, and add an additional level of tracking and traceability for vaccines as they travel through the supply chain.

Benefits are grouped into four primary areas:

- Storage capacity and scalability
- Accuracy and efficiency
- Product verification
- Regulatory compliance

Specific, more granular benefits and key takeaways exist within each of these groupings and these benefits differ across stakeholder groups. While the size of the impact of each benefit may vary by stakeholder, all members of the supply chain identified benefits associated with each of the broad groupings.

2.1.1 Storage Capacity

2D barcodes offer significantly more data storage capacity than linear barcodes. This means that more drug product attributes/data can be communicated via scanning a 2D barcode than from scanning a linear barcode. The use of 2D barcodes on secondary packaging allows for the lot number, expiration date, and unique product ID to be incorporated into a single data carrier. 2D barcodes also have sufficient capacity to meet future information demands, as well as to store supplemental data.

Along with enhanced storage capacity, 2D barcodes also provide scalability (i.e., ability to contain increasing amounts of data) with less resulting variability in image size. This means that additional data can be tracked on external packaging with limited impact to the size of the barcode itself. This consistency results in faster readability when compared to long linear barcodes, and provides more flexibility to store product information irrespective of available space on the packaging.[3]

2.1.1.1 Manufacturer

Based on the interviews conducted, manufacturers' main concern with respect to external data carriers is available space on the label. While space is less of a concern for secondary than primary packaging, there are still instances in which space constraints on external packaging make it difficult to fit product information. Serialization of products has the potential to intensify space constraints by adding standardized numerical identifiers (SNI) of up to 20 alphanumeric characters in addition to the national drug code (NDC), which will expand the size of the linear barcode.

The storage capacity of 2D barcodes allows the inclusion of a standardized numerical identifier, or other serialization identifier, in addition to product information such as lot number and expiration date, while maintaining a similar-sized data carrier. This uniformity allows for simpler, faster readability by downstream supply chain partners. While linear barcodes are capable, in theory, of encoding serialized identifiers, in doing so they become longer or require stacking to hold this additional data. Elongated or stacked linear barcodes would require significant additional space on the label, and the varying data amounts would result in barcodes of varying size. This would negatively affect readability and would increase the potential for errors during product scans.

2.1.1.2 Distributor

Given the volume of product that distributors manage, manual data entry of product information is excessively costly, and in many cases impractical. Manual data entry affects the quality of the information; data entry can often be inaccurate, and limits the amount of product information that distributors are capable of storing within inventory management systems. Sometimes distributors choose not to record the information at all. According to interviews conducted for this report, data such as expiration dates are not consistently stored and may have transposition errors due to different date formats (e.g., misread month as day). Product lot numbers are typically not stored at all. Encoding this information into 2D barcodes will allow distributors to consistently and accurately incorporate these data elements into their overall inventory management.

Due to the lack of such data being stored, current inventory management procedures inherently require manual processes related to recall, expiring product management, and short-

[3] GS1. "GS1 DataMatrix." GS1, n.d. Web. <http://www.gs1.org/docs/barcodes/GS1_DataMatrix_Introduction_and_technical_overview.pdf>.

date product management (i.e., selling soon-to-expire products at a discount or prioritizing their sale to the immunization community to facilitate product use in a timely manner). In the case of a product recall, once a recall alert is received from a manufacturer, distributors must manually verify each same-type product received from the manufacturer—this determines whether their current inventories are impacted by the alert. Additionally, the distributor needs to alert all purchasers of the same-type product, since the distributor will unlikely have an accurate record of the lot numbers of previously sold product. These alert processes are inefficient and potentially costly, as are the processing of returns.

Expiring product management and short-dating processes currently require similar manual data entry. Given that expiration dates are usually not stored within inventory management systems, distributors must verify expiration dates at the time of shipment. They also must conduct overall product expiration and short-dating management by manually checking the product inventory in their warehouses. Soon-to-expire product is therefore identified through monthly, weekly, or even daily "visual checks," during which such inventory is flagged and (if needed) the issue escalated via manual reports. These flagged products are prioritized for sale with discounts offered as a strategy to exhaust the expiring stock; however, the process does not allow for real-time expiree management, and impedes the ability of distributors to ensure that they are fully leveraging short-dating opportunities.

The additional storage capacity of 2D barcodes will enable distributors to incorporate lot numbers, expiration dates, and serialized numeric identifiers into their day-to-day inventory management operations. This additional product information enables more automatic processes and supports more efficient recall management. For example, as relevant inventory and sold product is identified within their systems, notifications can be directed toward customers who purchased or received compromised product. Additionally, expiration management processes can be conducted in real-time, enabling more effective short-date product management.

Combining these benefits with additional improvements to the returns, product distribution, and cycle counting processes may provide enough economic incentive to drive distributor adoption of 2D barcodes. 2D barcodes additionally provide the expanded data management capabilities that traceability will require.

2.1.1.3 Provider

Similar to distributors, there are currently many product data elements that providers do not track within their inventory management process. Due to the required effort and lack of multi-functional inventory management systems, many providers do not track important information such as lot number and expiration date in any meaningful way. While this information might be required to be included as part of a patient's medical records, it is often not entered into any system until the vaccine is administered.[4] As a result, these providers must conduct recalls and expiration management in a manner that depends heavily on manual processes.

Many large hospital systems could leverage lot-level information by storing it within currently available systems or modules that have the functionality to track product locations by lot number. They do not currently do this because this information is only included in human-readable form, and the amount of effort associated with manually entering the lot number for each unit would be untenable. Storing such information through automated data capture would provide the ability to expedite recall processes by quickly identifying the location of any product impacted by a recall alert, as diagramed in Figure 1. Physicians' offices and retail

[4] Centers for Disease Control and Prevention. "Fact Sheet for Vaccine Information Statements." Centers for Disease Control and Prevention, n.d. Web. <http://www.cdc.gov/vaccines/pubs/vis/vis-facts.htm>.

pharmacies may similarly benefit from being able to determine whether they have any inventory from a specific manufacturer and lot number. In either scenario, the addition of lot number information can potentially reduce manual processes.

Figure 1: Potential Provider Recall Process Enabled by Lot Number Storage

Adding expiration date tracking for vaccines would enable providers to queue vaccines that are expiring for use sooner rather than later. While there are currently processes in place to manage products effectively, these processes are not automatic and require manual review of inventory.

Providers may also benefit from the uniformity of 2D barcode size, which allows for a faster, more repeatable scanning process. This will help to mitigate learning curve concerns as practitioners confront less variability in terms of barcode size and shape. This consistency is critical in order to determine provider adoption of 2D barcode technology, which will be much more challenging without a simple, reliable scanning process.

Ideally, providers see value in further expanding the product information that is encoded within the external data carrier to include the manufacturer name, product name, total dosage, and the vaccine presentation type (i.e., multi-dose vial, package of pre-filled syringes). Encoding product NDC, serialized identifier, expiration date, and lot number will serve as a starting point. Doing so will encourage providers to begin expanding the data capacity of their inventory management systems and modernizing their inventory management processes to incorporate a multitude of data components. Data management modernization will facilitate building the capabilities required to support further expansion of the product information encoded and tracked within external data carriers.

2.1.1.4 Conclusion

Process changes and systems upgrades are an integral component of leveraging the benefits from additional data within 2D barcodes. Establishing functionality compatibility of current systems (e.g., Immunization Registries, EMRs, eMARs, and claims systems) will allow increased data availability, while incorporating new metrics into day-to-day operations will help better manage inventories and track product information.

2.1.2 Accuracy and Efficiency

The implementation of 2D barcodes on secondary packaging offers the entire supply chain the opportunity to improve the accuracy of the data entered into information management systems. Currently, downstream supply chain members (e.g., wholesalers, distributors, providers, and pharmacies) enter information such as vaccine lot number and expiration date manually into inventory management systems, pharmacy systems, and EMRs. Each manual entry creates the potential for introducing error, and may result in incorrect information ultimately flowing into an inventory management system or patient medical record. Reduction in manual data entry can result in fewer data entry errors and has obvious implications with respect to inventory control, recall management, and patient safety.

The CDC Vaccine Tracking System (VTrckS) "is an information technology system that integrates the entire publicly-funded vaccine supply chain from purchasing and ordering to distribution of the vaccine." VTrckS supports these capabilities in two ways: VTrckS Direct and as an interface to immunization registries software through VTrckS ExIS.

Both VTrckS Direct and VTrckS ExIS users have potential to benefit from the increased accuracy and completeness provided by 2D barcode scanning. Providers with access to VTrckS Direct could benefit from 2D barcodes on secondary packaging if VTrckS were modified to incorporate 2D barcoding scanning capabilities. Likewise, providers that directly record inventory on hand or vaccine administration data into an immunization registry that interfaces through VTrckS ExIS could benefit from 2D barcodes on secondary packaging if the immunization registry software were modified to incorporate 2D barcoding scanning capabilities.

Reduction in manual data entry processes also improves efficiency and accuracy. Ensuring that inventory management, payment systems, and EMRs are able to receive, process, and store 2D barcode data fields will expedite data capture processes for vaccines. For stakeholders managing large volumes of vaccines, even a marginal reduction in manual effort associated with each shipment or saleable unit can result in substantial decreases in overall labor costs.

2.1.2.1 Manufacturer

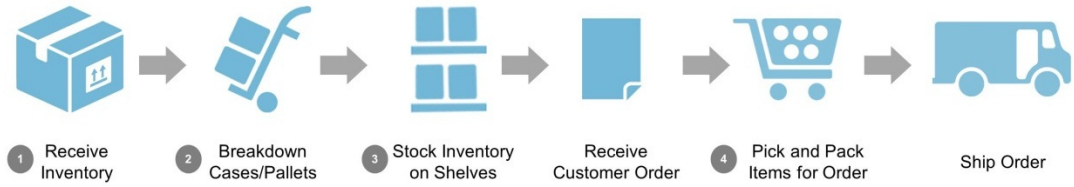
Manufacturers realize indirect benefits from the improved accuracy provided by 2D barcodes on secondary packaging. Improved accuracy increases the effectiveness of recall alerts by ensuring correct lot number tracking, and limits the potential impact of transcription errors by downstream partners. Ensuring that product information is stored accurately downstream improves the integrity of patient medical records and, as a result, improves patient safety.

Manufacturers have limited direct benefit from the accuracy and efficiency of 2D barcodes on secondary packaging; however, early adopters of 2D barcoded products may have a competitive advantage with providers whose processing time might be lessened with the new products. These providers would have an incentive to order items from the early adopters. Such a competitive advantage will, however, decrease over time. Additionally, altering external data carriers does not meaningfully impact current inventory management processes, as data are stored and managed without scanning individual barcodes. The data are already stored in the manufacturers' systems, either prior to or during production, and used to verify the accuracy of encoded data carriers.

2.1.2.2 Distributor

Leading distributors stated that they process upwards of 1 million vaccines daily. Most shipments are received in either pallets or cases, and are then broken down to the saleable level for storage. Orders from downstream customers are fulfilled by picking and packaging the required saleable units and shipping them typically in totes (i.e., plastic bins that are sealed) of homogenous or mixed products. The sheer volume of product requires an immense amount of inventory processing and tracking across each phase of the receiving, storing, and shipping processes. 2D barcodes can help distributors realize benefits throughout these processes as displayed in Figure 2.

Figure 2: Distributor Benefits Overview



2D Barcode-Related Benefits

1. Automated capture of product information
2. Aggregation-related efficiencies
3. Improved recall and short-dating management
4. Automated expiration verification

Increased automation can potentially provide reductions in labor requirements, ensure the integrity of product-related information storage within inventory systems, and assist product legitimacy verification. In addition, reduced time and effort during inventory receipt could potentially reduce labor costs and marginally reduce overall transportation time for vaccines (i.e., the transportation time is shortened by the more efficient and quicker inventory intake). In addition, improved data integrity will ensure distributors accurately respond to recall alerts and track inventory obsolescence in a much more meaningful and effective manner.

Limiting transcription errors or other manual processing mistakes for even a small portion of distributors' overall inventory could represent a considerable reduction in errors throughout the entire system. Similarly, negligible efficiency improvements, when multiplied by the total amount of inventory processed daily, could represent major efficiency gains.

2.1.2.3 Provider

Provider gains in data accuracy and unit-level processing efficiency would improve the inventory receipt process, save time, and increase the integrity of information tracked within patient medical records, internal inventory systems, and public health immunization information systems (IIS). In 2012, medical providers reported that "increased accuracy of records" was the most important factor driving them to use 2D barcode technology.[5]

Medical providers generally use either the secondary packaging of the product or leverage information from the purchase order slip to input product information into inventory management or immunization modules (if available), and EMR systems. For the latter, medical providers must still cross-reference the purchase order with the individual units in order to verify that the information is correct. Regardless of the source, this process is typically entirely manual (although sometimes NDC information can be scanned from the linear barcode—see Appendix 5.1), creating the potential for transcription errors.

Transcription errors may result from simple mistakes, or may occur because the human-readable content on the external packaging cannot actually be read. Content may be unreadable because the font is too small, the information is stamped, not printed in ink, or the content has been distorted or smudged during the distribution and storage process. Encoding information such as product NDC, serialized identifier, expiration date, and lot number within a data carrier on the secondary package will allow the bulk of product information to be entered into various systems with a single scan. This capability can reduce both human error

[5] RTI International. *Impact of a Two-Dimensional Barcode for Vaccine Production, Clinical Documentation, and Public Health Reporting and Tracking.* N.p.: Centers for Disease Control and Prevention, n.p., July 2012. PDF.

and the amount of time currently spent on manual data entry during the inventory receipt process.

The Brigham and Women's Hospital in Boston is a location where scanning has been used to help reduce manual errors and increase patient safety. In a study conducted at the hospital, researchers found that when no scanning was available, staff pharmacists picked an incorrect medication for their patient 2% of the time. While 69% of these errors were identified by a staff pharmacist prior to dispensing medication to the patient, the remaining errors were not detected prior to dispensing, resulting in an estimated 44,000 dispensing errors annually at this 735-bed hospital. Using bedside scans provided an additional, automated verification of medication being administered to a patient. It also ensured that medication data were easily and accurately uploaded to patient medical records during the dispensing process.[6]

Improving the accuracy of the data being stored by providers will not only impact internal inventory management and patient safety, but also help ensure the completeness and integrity of the data being reported to external bodies such as state or city IIS and others such as Vaccine Adverse Event Reporting System (VAERS), as well as federal programs such as the VFC program. Inevitably, inaccurate data at a provider level result in incorrect data being stored by these external entities that are reliant on the inputs they receive from providers. At a macro level, ensuring correct data at the point of administration, where either primary or secondary packaging may be used, is critical for management and assessment (e.g., adverse events) of the statewide and national vaccine supply chains.

The specific cost implications from time savings associated with automation directly correlate with the volume of product. Therefore, cost implications will differ for public health departments, physicians, and hospital groups. The use of 2D barcodes will almost certainly reduce time spent on the inventory receipt process (which typically occurs monthly for publicly purchased vaccines, and sporadically for privately purchased products). Additionally, physical inventory checks may be expedited as individual products can be scanned and verified against data stored within inventory systems and immunization models. This may result in reductions in labor costs, or simply free up medical practitioners to perform other responsibilities. In either case, providers should realize a benefit from less time consuming processes.

2.1.2.4 Conclusion

Infrastructure modernization and process enhancement throughout the vaccine supply chain is critical for ensuring that the potential for improved accuracy and efficiency is realized. Increased efficiency will help to offset broader cost increases from regulatory demands, such as exchange of e-pedigrees, while enhancements to data accuracy at any level will further promote patient safety.

2.1.3 Product Verification

Standardized Numerical Identifiers (SNIs) which the DSCSA requires as an encoded component of 2D barcodes secondary packaging, provide the potential for much more granularity in product tracking. Serialized 2D barcodes allow for product verification at the unit level (e.g., vial and/or syringes that can improve returns processes), and more specifically the chargeback process (i.e., refund process, if the units are sold at the same level). They also help identify potentially compromised vaccine products (i.e., recalled, contaminated, or counterfeit product) within the supply chain.

[6] Cooley, Thomas. Lessons Learned with Bar-coding and EMAR. N.p.: Brigham and Women's Hospital, n.d. PDF.

2.1.3.1 Manufacturer

Manufacturers typically do not handle the product returns and product disposal processes, as it is not best practice to receive products that have been out of their control back into inventory. The product returns and disposal functions are typically outsourced to third-party vendors who manage chargebacks[7] and the destruction of returned products. These third-party vendors may be able to use serialized product identifiers on secondary packaging to verify the integrity of chargebacks by linking returned product to specific purchases, thereby verifying the product source and correct purchase price. As a result, the vendors can identify whether a product was purchased privately or publicly at a discounted price, or if some other price reduction occurred. This helps to ensure that chargeback amounts are aligned with the price actually paid for the product.

Patient safety and brand integrity are principle concerns of manufacturers, who have every economic interest in preventing the counterfeiting of their products. Serialization enables product authentication at the point of sale or administration that would help catch counterfeit product before it reaches patients. Encoding serialized product identifiers allows providers to verify the authenticity of a product by querying the manufacturer to confirm the serial number. While not foolproof, this encoding provides an added layer of verification that helps to identify suspect product (i.e., product without a valid serial code) and protect patient safety.

2.1.3.2 Distributor

2D barcodes on the secondary packaging, especially when encoded with serialized data, can benefit distributors in terms of both returns processes and counterfeit identification.

From a returns perspective, distributors benefit from the same reimbursement improvements as manufacturers (i.e., a product can be tied to a specific purchase, therefore eliminating mismatches between purchase price and reimbursement amounts), and also benefit from verification of the source of the purchase. Unlike manufacturers, who in some cases may be the sole producer of a unique product, distributors are often one of many vendors for a plethora of different vaccines. Therefore, the chargeback process can be improved by verifying that returned products were actually purchased from the distributor making the reimbursement. By facilitating serialization, 2D barcodes would enable this verification and eliminate fraudulent returns to distributors made by bad actors.

Similar to manufacturers, distributors benefit in terms of patient safety and brand integrity to the extent that counterfeit products can be identified at the point of administration or sale and removed from the supply chain. Additionally, information encoded in the 2D barcodes on secondary packaging can help support more efficient product authentication for distributors' return process to manufacturers. Distributors need to provide additional information such as lot number and expiration date to manufacturers or their third-party logistics providers (3PL) to receive reimbursement. Having that information easily accessible on the product packaging enables distributors, manufacturers, and 3PLs to efficiently scan and acquire the required information.

2.1.3.3 Provider

Providers have limited benefits from 2D barcodes on secondary packaging that are serialized. The core value of serialization is the ability to authenticate product, and therefore improve

[7] Chargebacks are defined as when a wholesaler simple "charges back" the difference between a customer's contract price and the price that the wholesaler paid for the drug.

patient safety; however, aside from product authentication, the providers interviewed did not believe that serialization would be used in any meaningful way within inventory management or patient medical records. Since current processes are developed around lot numbers, providers see limited value from gaining the additional level of granularity that serialization provides. Please refer to Appendix A for a more detailed overview of the regulatory and legislative landscape.

2.1.3.4 Conclusion

Serialization is a potentially powerful tool against illicit activity within the supply chain. Aligning chargebacks with specific purchases will help to eliminate the potential for returns fraud. In addition, product authentication can add another layer in ensuring that the products moving through the supply chain are authentic. Still, product verification will require coordination across varying levels of the supply chain to ensure that proper checks are in place to authenticate products and purchases (e.g., providers will need to work with manufacturers to verify vaccine serial numbers).

2.1.4 Regulatory Compliance

The DSCSA places a clear emphasis on drug distribution security. Existing and developing DSCSA regulations will require changes ranging from serialized product identifiers to electronic product e-pedigrees and interoperable systems. All vaccine supply chain members will need to work collaboratively and creatively to ensure that the proper capabilities are in place to comply with the rapidly evolving regulatory landscape.

The FDA's 2010 SNI guidance recommends that manufacturers include "package-level" (i.e., saleable level) serialized numeric identifiers for prescription drug products. As has been previously discussed, the smallest saleable unit packaging in the case of vaccines is almost exclusively the secondary packaging. The increased data capacity of 2D barcodes makes the inclusion of serialized product codes plausible, and therefore addresses the requirements of the SNI guidance in a way that is relatively cost-effective for manufacturers (especially when compared to alternative solutions such as RFID technologies). Additionally, enabling serialized identifiers provides the initial foundation for the development of some form of e-pedigree system.

2.1.4.1 Manufacturer

As the producer of vaccines and their packaging, manufacturers bear the responsibility of ensuring that external artwork has the requisite information to meet regulatory demands, while also ensuring that the information is presented in such a way as to facilitate the efficient distribution of products down to the ultimate customers: patients. Both SNI guidance and e-pedigree regulations require the same basic capability: serialized product information. Compared to 2D barcodes, linear barcodes cannot encode serialized product information while also ensuring accurate and repeatable scanning processes. For all of the reasons previously discussed (e.g., storage capacity, scalability, efficiency), 2D barcodes offer a much more functional data carrier solution than linear barcodes.

Additionally, 2D barcode technology provides the functionality required for basic aggregation and inference by downstream supply chain members. 2D barcodes will allow manufacturers to use serialized identifiers so that downstream supply chain partners can infer transactional information for all saleable units within an aggregated group, and important elements for Track and Trace requirements. This helps to limit disruption to the supply chain, minimize distribution costs, and reduce the potential for product tampering and cold-chain temperature fluctuations (i.e., minimizing handling of cold-chain packages decreases likelihood of

temperature fluctuations). Manufacturers have a keen interest in making aggregation and inference as simple and cost-effective as possible.

2.1.4.2 Distributor

As the bridge between vaccine manufacturers and downstream supply chain members, distributors have unique exposure to regulations that affect vaccine-related transactions. Still, distributors have limited influence to affect the specific data carrier solutions selected by manufacturers to meet forthcoming regulations. Distributors must accommodate upstream technological changes while working to leverage the benefits and mitigate the challenges of these changes.

2D barcode technologies enable distributors to receive and transmit aggregated transactional information through storing serialized product hierarchies (i.e., a product's Pallet/Case/carton), which is a foundational requirement for meeting the demands of any e-pedigree system. Distributors can then use methodologies such as Six Sigma,[8] which use random sampling of shipments, to ensure reliability of the aggregated data received from manufacturers, and thereby avoid a costly forensic exercise for each shipment. 2D barcodes are therefore a viable option for meeting regulatory obligations.

2.1.4.3 Provider

Similar to distributors, providers may benefit from 2D barcodes as a means of meeting e-pedigree and serialization requirements. Additionally, the adoption of 2D barcode capabilities is acceptable to and expected by many leading hospital groups that have established agreements to support technological upgrades by leading manufacturers. These manufacturers have almost unilaterally indicated a shift to 2D barcodes. Therefore, adopting 2D capabilities in parallel with manufacturer adoption is necessary for these hospital groups to meet obligations in addition to regulatory requirements.

Table 1: Benefits Summary

	Manufacturer	Distributor	Provider
Storage Capability & Scalability	▪ Includes Standardized Numerical Identifiers (SNIs), lot number, and expiration date with similar-sized data carrier ▪ Smaller footprint than linear barcodes maximizes packaging real estate ▪ Scalable images accommodate current packaging artwork	▪ Able to store lot number and expiration date into data carrier and link to updated inventory management systems ▪ More efficient short-dating through improved visibility of product expiration ▪ Lot-level inventory tracking reduces manual labor during vaccine recalls ▪ Expiration date tracking helps prepare the shipping units (e.g., totes) more rapidly for shipment	▪ Consistent data carrier size enhances consistent readability ▪ Lot-level inventory tracking of product locations at facilities reduces recall time ▪ Additional information encoded in 2D barcodes (i.e., product name, manufacturer, dosage, vaccine presentation) could be used in future steps

[8] Six Sigma is a set of tools and strategies for process improvement originally developed by Motorola in 1985.Six Sigma seeks to improve the quality of process outputs by identifying and removing the causes of defects (errors) and minimizing variability in manufacturing and business processes.

	Manufacturer	Distributor	Provider
Accuracy & Efficiency	▪ Early adopters of 2D barcoded products may gain competitive advantage with providers whose processing time lessens with new products ▪ Increased downstream data accuracy and integrity improve patient safety	▪ Automated scanning receipt process potentially provides efficiency gains and less manual labor. ▪ Reduced reliance on manual expiration date check prior to shipments ▪ Increased data accuracy and integrity improves patient safety	▪ Scanning limits chance for transcription errors and improves patient safety ▪ Automated process expedites inventory receipt process ▪ Increased accuracy of data sent to state and federal programs and stored in EMRs ▪ Reduced time spent on physical inventory verification processes
Product Verification	▪ 2D barcodes encoded with SNI help verify the integrity of chargebacks ▪ Point of sale checks of serialized 2D barcode provide product authentication	▪ Serialized 2D barcodes coupled with traceability systems allow verification of purchase and price, which eliminates chargeback "mismatches" ▪ Serialized 2D barcodes support product authentication to identify potential instances of counterfeit vaccines ▪ Encoding additional data (e.g., lot number, expiration date) provides required information to manufacturers to facilitate reimbursement for returned product	▪ Potential patient safety benefit from product authentication
Regulatory Compliance	▪ Serialized 2D barcodes enable aggregation and inference which support e-pedigree ▪ Downstream trading partners will not have to open each aggregated product case, limiting opportunity for counterfeiting and cold-chain temperature fluctuations	▪ Serialized 2D barcodes enable aggregation and inference which support e-pedigree ▪ Distributors can use random sampling of shipments in order to ensure reliability of the aggregated data received from manufacturers, avoiding costly forensic exercises for each and every shipment	▪ Serialized 2D barcodes enable aggregation and inference which support e-pedigree ▪ Hospital groups have existing agreements with manufacturers to adopt 2D capabilities required to support data carrier changes made by manufacturers

2.1.4.4 Conclusion

2D barcodes are one of the few data carriers with the capability of carrying all of the data items needed to comply with governmental regulation. The technology is the choice of industry leaders, and provides the basic storage capabilities needed to address new laws and guidance. As the specific requirements take shape for each of the various supply chain members, the exact role that 2D barcodes might play in compliance will continue to become more clear.

2.2 Challenges of 2D Barcodes on Vaccine Secondary Packaging

Based on the potential benefits outlined in Section 2.1, the addition of 2D barcodes on secondary packaging offers opportunity and promise. Before stakeholders are able to realize these potential benefits, however, there are challenges that need to be addressed for adoption of 2D barcodes on secondary packaging.

Challenges have been grouped into three primary areas:

- Implementation costs
- Procedural changes
- Regulatory concerns

Specific, more granular challenges and key takeaways are presented within each of these groupings, and vary between stakeholder groups. While the impact of the challenge may vary by stakeholder group, all members of the supply chain have at least some challenges associated with each of the broad categories.

2.2.1 Implementation Costs

Supply chain members will need to make capital investments of infrastructure and system upgrades to create, verify and scan 2D barcodes and store their associated information. These investments range from printing, scanning, and verification equipment for manufacturers to produce vaccine packaging with 2D barcodes, to new handheld scanners and systems upgrades for providers to use the technology.

2.2.1.1 Manufacturer

The majority of vaccine manufacturers do not have 2D barcode printing capabilities implemented. Of the four vaccine manufacturers currently applying 2D barcodes, GlaxoSmithKline is the only vaccine manufacturer that has implemented 2D barcodes on secondary packaging as well as vaccine vials and syringes (as of August 2014). As such, significant investments will need to be made to print, verify, and affix 2D barcodes to secondary packaging across all vaccine product lines. A 2008 report on the economic impact of item serialization estimated the capital costs of implementing serialized 2D barcodes to be roughly $1.3 million per packaging line.[9]

Based on cost and procedural concerns, manufacturers will need to determine whether to print 2D barcodes online or offline. Online printing allows for increased flexibility, while offline printing minimizes the need for equipment upgrades on individual manufacturing lines. For uniform, un-serialized barcodes, offsite printing may by sufficient, but the looming reality of serialized data carriers makes static, bulk printing of barcodes a less viable alternative. Additionally, even without serialization, offline printing of individual barcodes or pre-printing of cartons may not be a scalable solution for some products.

In addition to printing and labeling equipment, manufacturers will need to purchase validation equipment (e.g., cameras) to verify the readability of their created 2D barcodes and validate their packaging data carriers. Infrastructure costs affecting manufacturers exceed those of providers, whose main equipment expenditures will likely be 2D barcode scanners, as opposed to printing machinery. Scanner replacement is far less expensive, while investment in new

[9] Forrester Consulting. Evaluating The Economic Impact Of Item Serialization: Concepts to Inform Advocacy. N.p.: Pharmaceutical Research and Manufacturers of America (PhRMA), n.p., Feb. 2008. PDF.

printing and quality verification equipment is both potentially costly and time consuming for manufacturers.

2.2.1.2 Distributor

Many industry-leading distributors already have some level of 2D scanning capability; however, they currently have insufficient 2D scanner capacity to support a complete industry shift to 2D barcodes for all vaccines. As a result, distributors will need to make investments in additional 2D-compatible scanners to facilitate expansion of their 2D scanning capacity. To ensure optimal efficiency, some distributors may need to upgrade previously purchased 2D scanners, as scanning times have been significantly reduced in the past few years. Given the large quantity of products that distributors handle, any scanning time reduction offers considerable time savings.

To the extent that the adoption of 2D barcode technology is gradual, 2D-compatible scanners can begin to replace linear equipment as part of equipment refreshes. Advance planning and budgeting of equipment upgrades and replacements can mitigate their cost to distributors. A more rapid transition between the technologies, however, would require a faster adoption of 2D scanning equipment. This would entail unanticipated capital expenditures outside of the normal equipment replacement cycle.

The required scanner costs ($250-350) are low compared to the cost of data management and data exchange software required for upcoming regulations. Distributors will require changes to their warehouse management system (WMS) systems to aggregate and de-aggregate the additional information encoded in the 2D barcodes. They will also require new interfaces development between the WMS and the product transfer solutions in order to build the detail required to meet DSCSA e-pedigree regulations. It is possible that potential costs associated with infrastructure upgrade, scanning equipment, and systems may be passed on to the marketplace.

2.2.1.3 Provider

Currently, providers cover the spectrum in their use of scanners for information capture. The majority of physicians and public health departments do not use the NDC linear barcode on the secondary packaging and do not have the ability to scan any barcodes at their offices. Some larger medical practices and hospital groups already have scanning capabilities and use this functionality in inventory management, bedside patient administration of vaccines, or both.

Providers also vary in their ability to afford 2D scanners. Hospital groups may have less capital restrictions, whereas public health departments may be unable to buy scanners without initiatives to help subsidize the cost. Besides scanner costs, the limited number of vaccines with 2D barcodes on secondary or primary packaging reduces incentives for providers to purchase the required scanners.

Some providers such as hospital groups already own and use 2D scanners for internal use to input information into patients' EMRs. Even in those cases, however, using scanners for inventory receipt of all vaccine products would require additional scanners and integrated inventory management systems—systems that could automatically capture the information from the secondary packaging 2D barcode.

A major internal challenge for providers is getting software vendors to implement scanning systems to interface and record the scanned data from the barcodes into existing inventory management and EMR systems. It is unclear how long the integration process will take, and concerns exist that the process will be costly and time-consuming. Without the ability to interface the data with their information management systems, the benefits associated with 2D

barcodes are limited or even non-existent for providers. Some EMRs have the capability to also manage inventory but do not store all the information that would presumably be in the serialized 2D barcode. To fully use 2D barcodes on secondary packaging, providers would need to work with EMR vendors to increase functionality in their EMR systems.

An important issue that will require the vaccine industry's attention is how to help providers fully benefit from 2D barcode technology if they cannot afford scanners and the associated technology necessary to fully use such tools. Additionally, providers may need to purchase e-pedigree software once DSCSA requirements come into effect.

2.2.1.4 Conclusion

Implementation costs vary between different stakeholder groups. Even within these groups, implementation costs differ due to varying current capabilities relative to 2D barcode production or scanning. These upfront capital investment costs represent a sizeable challenge for any new data carrier technology, and as such, are a key consideration as various stakeholders allocate capital budgets and prioritize financial investments in the coming years. While these implementation costs may represent the initial hurdle for new technology adoption, procedural changes pose sustained challenges for stakeholders that must adjust, and in some cases redesign, current processes.

2.2.2 Procedural Changes

The ability to scan and store 2D barcode information is a crucial component of transitioning away from linear barcodes; however, it is only one part of achieving functionality and usability. An equally important step towards utilizing 2D barcodes on vaccine secondary packaging is making the procedural changes required to accommodate their use in inventory receipt and management. A main procedural concern from industry-wide adoption of 2D barcode technology is the management of varying data carriers within inventory during the transitional phase of linear to 2D barcodes on vaccine secondary packaging.

2.2.2.1 Manufacturer

Manufacturers will have to change some of their current processes as they add 2D barcodes on secondary packaging of vaccines. Changes range from printing and encoding 2D barcodes to getting FDA approvals to dealing with exception handling when 2D barcodes are not encoded correctly or are unreadable.

One of the first challenges manufacturers will have to resolve is how to print the 2D barcodes on vaccine packaging. Due to the increased data density and complexity relative to linear barcodes, 2D barcodes require additional emphasis on precise printing. Printing 2D barcodes on vaccine secondary packaging is further complicated by the variable temperatures associated with cold chain vaccines. Additional testing and verification is required to ensure that the 2D barcode will be readable despite temperature fluctuations and condensation. One manufacturer interviewed indicated that they were utilizing laser-etching technology as opposed to ink-jet printing for this specific reason. Manufacturers also indicated that certain alternatives such as offline, pre-printed barcodes and manual stickering were not viable, scalable solutions that could support serialization requirements and meet manufacturing needs.

Another challenge which manufacturers have to address is creating 2D barcodes using industry-accepted standards. All manufacturers interviewed have decided to encode their

barcodes using GS1 standards, which provides guidance for how to encode information in a uniform manner. In March of 2013, GS1 released an implementation guideline,[10] which will guide the industry on leading practices for encoding and supply chain management for e-pedigree. GS1 standards, however, are only effective insofar as their interpretation and execution is uniform across the industry and support interoperability. A potential concern is that misinterpretation of standards may result in miscoded barcodes and an inability to properly read data from them by downstream users. This may happen during their initial use of 2D barcoding, since the packaging engineers are unfamiliar with GS1 standards and their configuration.

Some leading manufacturers participating in 2D barcode pilots have expressed that encoding 2D data carriers, even with GS1 standards guidance, can be much more complex than encoding linear barcodes. Manufacturers need to ensure alignment in terms of standards interpretations, and concerning the data points being included within the barcode.

Downstream trading partners expressed apprehension that the information encoded within secondary barcodes may vary across manufacturers, thereby further complicating and lengthening the inventory scanning process, and the ability of their inventory systems to properly categorize different data fields.

DSCSA takes steps to address this concern by detailing the data elements required for e-pedigree. DSCSA does not however address variability in lot number conventions specific to certain vaccines, which will pose a challenge for accountability when 2D scanning is used at the vial/syringe level. An example of lot convention variability would be a vaccine using a special character in the lot number to indicate packaging level - for example, 123A2 for the lot number of the vial and 123B2 for the lot number of the related secondary packaging. The variance in lot numbers requires EHR/IIS systems to implement special logic to relate the scanned vial lot number to the secondary packaging lot number entered into inventory. The absence of this EHR/IIS logic makes decrementing inventory when a vaccination encounter occurs challenging.

Another issue that needs clarification with downstream trading partners is whether manufacturers will retain linear barcodes on their vaccine secondary packaging in addition to a 2D barcode, or adopt 2D barcodes in place of current linear barcodes altogether. Manufacturers can obtain a waiver from the FDA to replace their linear barcodes on vaccines with 2D barcodes, and some manufacturers intend to print only 2D barcodes. The majority of manufacturers plan to transition to solely printing 2D barcodes on vaccine secondary packaging eventually, but in the interim will maintain linear barcodes for downstream partners. Distributors and manufacturers, however, are not entirely aligned in terms of what their expectations are for the timeframe for retaining linear barcodes on secondary packaging, nor with how to plan for the eventual change away from linear barcodes altogether.

Once manufacturers decide to begin implementing 2D barcodes on secondary packaging, they will need to get approval from the FDA for all label, product line, and software changes. FDA approval can take varied amounts of time depending on the variety of changes and the time of submission (e.g., annual process, ad hoc request). It is important to note that as the industry seeks to convert its artwork within the next three years, the FDA could be backlogged with approval requests that could further delay implementation timelines.

Manufacturers will need to coordinate the release of 2D-encoded vaccine products with downstream supply chain partners. Some manufacturers use third-party logistics companies

10 http://www.gs1us.org/about-gs1-us/media-center/gs1-us-press-releases/healthcare-guideline

(3PLs) to handle their distribution. In these cases, the manufacturer has a contract with the 3PL that includes required equipment purchases for manufacturer product distribution. Switching to solely 2D barcodes on vaccine secondary packaging may require certain manufacturers to re-contract with their 3PL to buy and use 2D scanners for their vaccine products.

DSCSA product transaction information, transaction history and transaction statement maintenance will add an additional layer of complexity to manufacturer processes. Discussions regarding this type of exception handling for mis-ships or inability to read packaging labels do not yet seem fully mature. The risk for manufacturers is that such exceptions might result in withheld payments. This, in turn, would result in manufacturers holding the monetary risk of e-pedigree exceptions, which would require them to maintain financial reserves to account for potential lost revenues.

2.2.2.2 Distributor

Distributors' role within the supply chain includes the receipt of products from several different manufacturers, which exposes them to the potential for significant inventory management disruptions if encoding standards are not followed. During a transitory period to 2D barcodes, a natural learning curve is to be expected, where the increased complexity of 2D barcodes and adjustment to new standards may result in miscommunication or errors in encoding by manufacturers. Sustained variances will have significant adverse impacts on distributors.

As they aim to ensure a functional system, manufacturers and distributors need to agree on the desired printing grade of 2D barcodes on the secondary packaging. Print grades are determined by an American National Standards Institute (ANSI) test, which ranks labels from A to F, based on a 0.0 to 4.0 scale. GS1 standards require print quality of Grade C or higher, and the FDA barcode ruling incorporates this requirement by reference.[11] In theory, a drug package with less than a "C" grade barcode can be declared "mislabeled" and be subject to recall if it is not readable. For this reason, distributors clearly stated that for optimal use of 2D barcodes, they might require Grade B quality printing in order to ensure proper scanning. If manufacturing print grades are not up to distributors' preferred grade requirements, disruptions in the distribution chain may occur due to unreadable barcodes. Additionally, distributors may impose financial penalties on manufacturers who do not comply with their quality requests to account for costs associated with procedural disruption. Enhanced communication, transparency, and education between distributors and manufacturers will be needed to effectively address such issues going forward.

While scanners can be programmed to read barcodes based on GS1 standards, the time associated with reading the barcode increases when determining varying elements and sequences. In some cases, the amount of time required for scanning a 2D barcode is already longer than scanning a linear barcode. According to our stakeholder discussions, an internal distributor study that was conducted four years ago found that linear barcodes take 0.01 seconds to read compared to 0.7 to 1.2 seconds for 2D barcodes. Adding time to configure scanners to interface with existing systems and product variations will lengthen that time even further. In a business where large volumes of product are scanned every day, this increase in scanning time could potentially cause large delays for distributors. Industry standards need to be adopted in order to align standards with distributors' functional concerns.

During pilot testing, interviewed distributors mentioned that switching back and forth between linear and 2D scanning on the same product (accomplished by switching scanner settings)

[11] *http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/UCM267392.pdf*

caused inefficiencies and productivity loss. Distributors managing a supply chain being flooded with a mix of different data carriers on external packaging face increased inefficiencies and sporadic downtimes. Given the current low volume of 2D barcodes within the supply chain, many distributors have addressed this issue by choosing to invest in multiple scanners with some programmed specifically for linear and others programmed solely for 2D. This, however, becomes less financially feasible as the mix of data carriers grows during the transition phase. Distributors will need to work in conjunction with manufacturers to ensure that data carriers are uniform across each product and that the expectations are aligned with respect to the data carriers anticipated on inventory when it is received.

The inclusion of multiple barcode types (providing both linear and 2D barcodes on the same product) requires downstream supply chain members to ensure that sufficient procedures and trainings are in place for employees and systems to delineate between when to use one data carrier versus another. Inadvertent use of the wrong data carrier might result in redundant effort and incorrect or incomplete data capture. Efficiencies associated with encoding additional data within 2D barcodes could easily be offset by additional labor effort and costs from incorrect scans.

If linear barcodes are removed from vaccine secondary packaging altogether, there would be pressure on downstream supply chain members to rapidly expand their capacity to handle 2D barcodes within a short timeframe. Under this "flip the switch" scenario, the costs associated with infrastructure upgrades would be the highest, since replacement of current scanners would take place during a more limited timeframe. Additionally, this change would greatly shorten the process change timeline, thereby increasing the potential impact of learning curve risks.

Once distributors begin to pass e-pedigrees further downstream, many potential exception situations can be imagined. Some examples include distributors being unable to read serialized 2D barcodes, or incorrect aggregation (i.e., erroneous parent-child relationships) by manufacturers. These exceptions would prohibit distributors from further selling the disputed items downstream, causing potential delays in getting vaccines to consumers. Manufacturers and distributors will work together to follow DSCSA exception handling procedures in order to mitigate potentially costly issues such as un-saleable product resulting in drug shortages.

2.2.2.3 Provider

Providers serve as the last trading partner in the supply chain and are therefore the recipients of any upstream changes. The addition of 2D barcodes on secondary packaging may cause inventory receipt and scanning process changes for them. Additionally, the relationship between secondary and primary packaging NDCs must exist in provider systems to ensure scanning of vials and syringes appropriately decrements inventory. Providers will also be affected by the quality and placement of the barcode on vaccine secondary packaging.

The inclusion of multiple data carriers (i.e., a linear barcode and a 2D barcode) would present many of the same challenges to providers as it would to distributors. The main issue is that very few providers have the capability to scan 2D barcodes, with some not even able to scan linear barcodes. To realize the full benefits of 2D barcode technology, providers must be prepared to work with 2D barcodes. Widespread adoption of 2D capabilities is less likely if the usage of 2D barcodes is not universal, and if there is a sizable mix of both linear and 2D barcodes on packaging.

To ensure that the 2D barcodes are used correctly, clinicians need to recognize 2D barcodes and know when to scan them. Additionally, when clinicians receive mixed inventory of linear and 2D barcodes on vaccine secondary packaging, they need to be educated on different

processes for each type of barcode. In many cases, providers may have a scanner that can only read linear barcodes and therefore, whenever they receive vaccines with secondary packaging containing a 2D barcode, they might need to revert to a manual process to enter the data. A provider who used 2D barcodes on vaccine secondary packaging mentioned that the process of switching between scanning 2D barcodes and manual entry was cumbersome.

Another issue to be discussed by providers and standardized at an industry level is what to scan for different parts of a multi-component vaccine. There is confusion and varying procedures in place since the NDC numbers, lot number, and expiration date on the secondary packaging versus the vaccine components can be different. Industry-wide standardization of the information contained on the secondary packaging 2D barcode will help simplify this process and standardize it.

An issue of equal importance to providers is the placement and quality of the 2D barcodes on vaccine secondary packaging they receive. Currently, barcodes are placed in differing locations on the secondary packaging. They can be on the top, bottom, or sides of the package. This causes two main challenges for providers. First, the sides and tops of vaccine secondary packaging are occasionally ripped off before placement in the refrigerator, resulting in lost barcode information. Second, upon receipt of the vaccine, providers need to scan the 2D barcode on the secondary packaging to input it into their system, and the longer it takes to find the 2D barcodes, the longer amount of time cold chain vaccines are out of the refrigerator in varying temperature. Therefore, providers have voiced their preference to have 2D barcodes in a standardized location on vaccine secondary packaging, preferably on the front face of the packaging.

The durability of the 2D barcode is also of essential importance to providers. Providers recounted situations where the boxes of refrigerated vaccines became soggy and the barcode on the box unreadable by their scanners. This results in additional manual work for providers and takes away from efficiency gains fostered by 2D barcode scanning.

Standardization is also needed in vaccine storage processes to achieve full efficiency and accuracy gains from 2D barcodes on vaccine secondary packaging. Currently, some providers are storing vaccines in their secondary packaging whereas others store them in their primary packaging only. If providers do not store the vaccines in their secondary packaging, the information encoded in the 2D barcodes will not be available to be used for returns processes or information retrieval (i.e., in cases where the vaccine syringe is accidently thrown away before being scanned at point of administration).

Table 2: Challenges Summary

Manufacturer	Distributor	Provider

Implementation Costs	▪ Need to purchase equipment (line management, vision, labeling, validation), and e-pedigree software ▪ Depending on the product, offline printing or pre-printing cartons would not be a scalable solution	▪ Need to increase 2D scanning capacity via purchase of additional scanners ▪ Changes necessary to inventory management systems, especially when handling serialized product for traceability purposes ▪ Potential cost increases passed on to marketplace	▪ Not all providers (e.g., public health departments) can afford 2D scanners ▪ Not all EMRs that incorporate 2D scanning abilities may make them a standard feature. ▪ Limited current use of 2D barcodes reduces incentive to adopt 2D scanners early ▪ Inventory systems and EMRs have limited ability to map 2D information; need to increase functionality ▪ Without the ability to interface the data with information management systems, 2D barcodes benefits are limited (if not non-existent)
Procedural Changes	▪ Need to ensure that variable vaccine storage temperatures do not distort barcode image ▪ GS1 standards 2D barcodes learning curve ▪ Changes (e.g., label, product line, software) take time for FDA approval (e.g., annual process, ad hoc)—all packaging approvals concurrently could backlog FDA ▪ Need to re-contract with dedicated 3PL providers to ensure compatibility with 2D barcodes ▪ Many manufacturers want to adopt 2D barcodes with human readable in near future—could have downstream trading partner effect ▪ Uncertainty about who will hold monetary risk of exception handling	▪ Industry standards require Grade C barcodes; distributors require Grade B for functionality (i.e., upstream education needed) ▪ Employee training required for knowledge when to scan using linear vs. 2D barcodes ▪ Mixed inventory currently requires switching scanners, reduces productivity ▪ Much faster adoption required if manufacturers transition straight to 2D barcodes only ▪ DSCSA is still working to standardize requirements for exception handling and rework (e.g., case breaks open) product transfer.	▪ Cumbersome to switch between manual entry and scanning if not all barcodes are 2D ▪ Clinicians need to recognize what to scan (i.e., learning curve) ▪ Need to determine how to scan varying information for different parts of multi-component vaccine ▪ Potential for soggy boxes to distort 2D barcodes ▪ Placement of barcodes important because sides and tops are ripped off occasionally; prefer front-faced placement ▪ Some providers do not retain secondary packaging when they store product (i.e., store in primary)
Regulatory Concerns	▪ Shrinking window for pilots or gradual introduction of 2D barcodes ▪ Industry-wide orders of planned equipment and implementation resources (including software resources) at same time may create supply constraints ▪ Need to coordinate contract manufacturing and packaging partners adoption of 2D barcode capabilities in order to meet regulations ▪ Manufacturers plan to make significant capital commitments across 2013, 2014, and 2015, so federal preemption impact may be limited (if capital investments have already been made in infrastructure upgrades)	▪ Expedited adoption timeline limits ability to replace scanners during normal equipment refresh and mitigate costs ▪ Providers paying little attention to transition due to deferred adoption timeline; unlikely to participate in many pilots ▪ Distributors adoption tied to manufacturer decisions and changes	▪ Limited, if any, current 2D scanning capabilities (i.e., some not scanning even linear barcodes) ▪ Expedited adoption timeline limits ability to replace scanners during normal equipment refresh and mitigate costs ▪ Providers not currently considering legislation, awaiting imminent adoption and potential Federal preemption o

2.2.2.4 Conclusion

The process changes required to implement 2D barcodes throughout the vaccine industry are far from insignificant. Manufacturers will need to alter how they produce product packaging, distributors will need to adopt new capabilities for receiving and managing massive quantities of vaccine products, and providers will have to reevaluate how they use secondary packaging as its utility is improved with additional encoded information. Getting such process changes right will require education, training, investment, and tremendous effort. This is a significant undertaking, and one only further complicated by the upcoming timeline dictated by DSCSA.

2.2.3 Regulatory Concerns

2.2.3.1 Manufacturer

DSCSA requires that manufacturers have the ability to send and receive Transaction Information, Transaction History, and Transaction Statements by January 2015. Additionally, DSCSA requires manufacturers to have applied serialization to saleable units before November 2017. This fast approaching deadline has reduced the amount of time for manufacturers to gradually introduce 2D barcodes on secondary packaging. It also limits their opportunities for conducting pilots both internally and with their trading partners. Each of these pilots can take as long as 12 months to complete, an issue further compounded by the fact that nearly half of pharmaceutical manufacturers polled in October 2012 had not yet initiated any sort of 2D barcode pilot.[12]

Given the upcoming deadline, manufacturers plan to make significant capital commitments to address the challenges over the next few years. Manufacturers not only have to update their own plants and software for e-pedigree regulations, but some manufacturers also work with contract manufacturing and packaging partners and will need to ensure that these partners also adopt 2D barcode capabilities in order to meet regulations.

Additionally, some manufacturers raised the concern that there is a limited pool of companies that produce 2D manufacturing equipment and a long lead time to procure such equipment. As a result, a compressed industry-wide implementation may result in equipment shortages, delayed order fulfillment, and late installation. There are also a limited number of vendors who have established e-pedigree software for manufacturers. The shortage of resources needed to address DSCSA regulations may pose a challenge to manufacturers in meeting the 2017 serialization deadline—or having to pay significant premiums for certain equipment and services.

2.2.3.2 Distributor

DSCSA requires serialization compliance by distributors by November 2019. The predominant driver for the adoption of 2D barcode capabilities for distributors, however, is the use of 2D barcode technology by manufacturers. All vaccine manufacturers will have applied 2D barcodes to their vaccine saleable level cartons by or before November 2017. If manufacturers decide to replace linear barcodes on vaccine secondary packaging with 2D barcodes, then distributors will be under pressure to increase their 2D barcode scanning capabilities and capacities by 2015.

Another challenge for distributors is providers' lack of interest in working with them to pilot e-pedigree related projects. DSCSA requires providers to track Transaction History, Transaction Information, and Transaction Statements by July 2015. Providers are not required to transact

[12] Healthcare Packaging. *Pharmaceutical Track-And-Trace Serialization Playbook*. N.p.: Healthcare Packaging, 2013. PDF.

with products without a product identifier until November 2020, meaning providers have little incentive to start working with their trading partners on a transition at this time (as of August 2014). As the intermediaries between manufacturers and providers, distributors will want to work on comprehensive product and process flow pilots that demonstrate the traceability of products from manufacturers all the way to providers in the supply chain. Distributor adoption of systems and scanning technologies is almost entirely tied to manufacturer decisions.

2.2.3.3 Provider

Currently, many providers have limited, if any, scanning capabilities. Even fewer providers possess 2D scanning capabilities. Most providers are not currently considering the effects of DSCSA (i.e., serialization for all returned drug packages, and required e-pedigrees for prescription drug products), given the long timeframe until they need to meet regulations. Providers may also need to invest in EMRs/systems and hardware in order to read and consume data encoded in a 2D barcode.

Current regulatory timelines offer little incentive for providers to work in conjunction with upstream stakeholders to implement changes in the near future. Absent provider input, manufacturers and distributors are forced to make decisions based on what they think providers' needs are, but without fully understanding those needs. This puts providers at a disadvantage and raises the possibility of a sub-standard solution. To address this issue, providers need to begin having serious planning discussions regarding forthcoming e-pedigree requirements well in advance of statutorily determined adoption deadlines.

2.2.3.4 Conclusion

DSCSA currently provides guidance on regulations and timelines. The regulation is evolving to address the finer points of supply chain requirements in consultation with industry representatives. Supply chain stakeholders must evaluate the requirements posed by current DSCSA requirements and make decisions regarding 2D barcodes based on the information available.

3 Key Findings

Over the course of assessing inputs from both external research and conversations with leading industry stakeholders, several key points have become evident. While not intended to be a comprehensive summary of the report, these key points represent independent observations that hopefully provide additional perspective regarding the potential adoption and impact of 2D barcodes on secondary packaging for vaccines. While derived from facts and industry perspectives, the specific observations made from this information are subjective in nature.

2D barcodes will become the industry standard for vaccine secondary packaging in the next three years

The current regulatory climate has made increasingly apparent the inevitable end of linear barcode usage within the vaccine industry. Shifting functional concerns, coupled with practical cost and process considerations, have led to an industry-wide consensus that 2D barcodes will eventually become the new standard for secondary packaging on vaccines. Ongoing hurdles for RFID technology have negated it as a possible alternative for secondary packaging, while recent pilot projects involving 2D barcodes for both primary and secondary packaging have increased vaccine manufacturer familiarity with the 2D technology. As track and trace and serialization requirements come into effect in the next three years, 2D barcodes will become the industry standard for vaccine secondary packaging. Similar looming requirements in global markets, such as Europe, will drive global adoption of 2D barcodes as the industry standard over the next decade.

Improved inventory management will be the main benefit to downstream supply chain members

While primary packaging labels are predominantly used to input information into patient medical records, secondary packaging can be instrumental in supporting efficient tracking and management of product inventories. 2D barcodes on secondary packaging provide improved accuracy and efficiency during the inventory receipt process, and encourage more advanced inventory tracking by automating the capture of additional data elements such as lot number and expiration date. By fully leveraging 2D barcode technology, distributors and providers can expedite the receipt process, enhance short-dating capabilities, and ensure less reliance on manual effort during recalls.

The full scope of this benefit, and ultimately the value of 2D barcodes on secondary packaging, varies by stakeholder in proportion to the size and complexity of their vaccine inventories. Distributors and larger providers who manage large quantities of vaccines will realize significant value from increased automation and management of inventories. Conversely, smaller providers who administer limited amounts of vaccines will likely realize less value from automation and may be less incentivized to incur the costs and process changes necessary to leverage 2D barcode technologies. Instead, they may opt to continue managing vaccine

inventories manually. Additionally, manufacturers have limited benefit in terms of inventory management from changes to data carrier technology since this product information is already entered into inventory management systems during the manufacturing process.

Regulatory uncertainty stalled adoption of 2D barcodes on vaccine secondary packaging

Despite general agreement on the eventuality of 2D barcodes on vaccine secondary packaging, lack of regulatory certainty hampered its adoption. The passage of DSCSA removes the uncertainty of whether a federal or state-based model will stand. Stakeholders, unwilling to institute significant changes without clarity regarding state and federal requirements for drug distribution security, and more specifically tracking and tracing of vaccine products now have the direction required to move forward.

Current lack of coordination in the vaccine supply chain complicates adoption of 2D barcodes and impedes full use of the technology

Industry associations have initiated conversations regarding changes, and supply chain members have conducted limited pilots to test the technology, but these efforts have been far from comprehensive or sufficient in addressing the full scope of 2D adoption considerations. Manufacturers' anticipated timelines for adoption vary significantly from one another within the DSCSA window of now until November 2017. There is no uniformity on certain core issues such as whether 2D barcodes will be included in addition to or in place of current linear barcodes. Distributors do not have a clear understanding of manufacturers' anticipated adoption timelines and have unresolved concerns regarding the minimum acceptable printing grade of 2D barcodes.

Until recently, providers for their part have been largely excluded from discussions. With limited exceptions, providers and provider software vendors have not participated in pilot programs, leading to a dearth of true end-to-end pilot programs that assess 2D barcode technology on secondary packaging. Providers have also had very few internal conversations regarding the adoption of any new scanning technologies on secondary packaging. Neither have they assessed how these technologies might be integrated with current EMR systems or the role that secondary packaging might play in meeting DSCSA requirements.

In order for 2D barcodes to be effectively implemented to fully enable all of the potential benefits of the technology, the vaccine industry will need to approach the issue holistically. This means aligning expectations through collaboration and transparency of adoption timeframes so that supply chain members can make necessary investments in software and hardware to support 2D barcodes. It also means making sure that downstream supply chain members, including small-scale medical providers, have the means and incentives to properly prepare themselves with the necessary infrastructure to take full advantage of the technology.

Several small providers have limited financial resources available to invest in 2D barcode scanning equipment. They are furthermore reliant upon EMR vendors to update the systems and provide the necessary functionality to leverage the 2D barcode information from a more automated data capture process. The entire vaccine industry has a stake, in terms of supply chain safety and efficiency as well as patient safety, to ensure that all members of the supply chain can use 2D barcodes—to improve both data accuracy and vaccine distribution efficiency. How the supply chain ensures that all of its members can use 2D barcode technology will be an important consideration well into the future.

4 Recommendations

Much remains unclear regarding the specific timeframe for the adoption of 2D barcodes on the primary and secondary packaging levels of products. Uncertainty with respect to how various stakeholder concerns are addressed remains high as well. There are, however, several actions that industry members and regulators could take to further assist the adoption of this technology.

Industry-wide stakeholder engagement is required to ensure an effective transition

Federal regulatory agencies and industry stakeholders need additional conversations to address concerns related to unresolved issues such as minimum print grade requirements, exceptions handling for unusable or damaged 2D barcodes. The FDA recently held periods for open comment and has convened workgroups to broaden considerations of these additional elements. Education and outreach about these workgroups and regulatory evolution is recommended to engage all stakeholders and help them understand the potential implications of 2D use.

End-to-end 2D barcode pilots can improve provider engagement and identify additional stakeholder adoption concerns

While some 2D barcode pilots have been conducted between manufacturers and distributors within the prescription drug industry, increased engagement with health care providers is essential in order to address their specific adoption concerns. Thus far, vaccine provider engagement as part of 2D pilot programs has been limited to CDC's 2D pilots. End-to-end 2D barcoding pilots that test barcode functionality on vaccine secondary packaging from the point of manufacture all the way to the point of administration would provide a better understanding of the full scope of benefits associated with the change. Additionally, end-to-end pilots could help identify additional considerations across the vaccine supply chain and accelerate discussions regarding adoption of the technology. Given the sheer volume of providers, as well as their current lack of adoption preparedness, manufacturers and large-scale distributors will need to play a proactive role in developing these pilot programs and in enrolling providers to participate.

- **Evaluate the value of retaining linear barcodes:** Distributors and manufacturers, however, are not entirely aligned in terms of what their expectations are for the timeframe for retaining linear barcodes on secondary packaging, nor with how to plan for the eventual change away from linear barcodes altogether.

- **Encourage adoption and transition to scanners that can read multiple types of barcodes, including images:** In many cases, providers may have a scanner that can only read linear barcodes and therefore, whenever they receive vaccines with secondary packaging containing a 2D barcode, they might need to revert to a manual process to enter the data. A provider who used 2D barcodes on vaccine secondary packaging mentioned that the process of switching between scanning 2D barcodes and manual entry was cumbersome. The key will be to balance the cost of the scanners with

the utility, or to seek alternative scanner technology and capabilities such as smartphone scanners with supporting application software.

- **Standardize multi-component vaccine barcoding and scanning processes:** Another issue discussed by providers and standardized at an industry level is what to scan for different parts of a multi-component vaccine. There is confusion and varying procedures in place since the NDC numbers, lot number, and expiration date on the secondary packaging versus the vaccine components can be different. Industry-wide standardization of the information contained on the secondary packaging 2D barcode will help simplify this process and standardize it.

- **Encourage manufacturers to work with their customers to provide consistent placement, quality, and orientation of barcodes:** An issue of equal importance to providers is the placement and quality of the 2D barcodes on vaccine secondary packaging they receive. Differing barcode placement causes two main challenges for providers. Because the sides and tops of vaccine secondary packaging are occasionally ripped off before placement in the refrigerator, barcode information can often be lost. Additionally, upon receipt of the vaccine, providers need to scan the 2D barcode on the secondary packaging. Without standard placement, it takes additional time to locate the 2D barcodes and may result in cold chain vaccines remaining in varying temperature. Providers have voiced their preference to have 2D barcodes in a standardized location on vaccine secondary packaging, preferably on the front face of the packaging.

- **Modify inventory data retention abilities in the provider space:** If providers do not store data encoded on secondary packaging, then it will not be available to be used for returns processes or information retrieval (i.e., in cases where the vaccine syringe is accidentally thrown away before being scanned at point of administration).

System vendors' engagement will facilitate inventory management and EMR solutions to leverage 2D barcode benefits

A key component of stakeholder adoption is the ability to leverage 2D barcode data within their current inventory management and EMR and PMS systems. Vendors of these systems will need to be engaged in order to ensure that they provide sufficient guidance on required functionality within these systems to capture and use additional encoded information such as lot number, expiration date, and serialized product identifiers. Stakeholders will need to work with systems vendors to develop requirements and encourage upgraded system functionality

- **Establish functional requirements for users and solution providers:** A potential concern is that misinterpretation of standards may result in miscoded barcodes and an inability to properly read data from them by downstream users. This may happen during their initial use of 2D barcoding since the packaging engineers are unfamiliar with GS1 standards and their configuration. It is also important that this data can be consumed by receiving systems, including EMRs, PMS, electronic medication administration record (eMAR), and pharmacy systems and, by providing a foundational set of requirements, they can build the capability into future enhancements.

- **Develop barcode validation/testing certification services:** Downstream trading partners expressed apprehension that the information encoded within secondary barcodes may vary across manufacturers, thereby further complicating and lengthening the inventory scanning process, and the ability of their inventory systems to properly categorize different data fields. Confirmation or verification of barcode integrity, quality, and consistency would support alignment across hierarchies and manufacturers. While

there are implementation guides available in the industry today, the guidance is based on the experiences of a few and is not widely accessible. Education and further piloting over time will enhance and improve understanding.

Develop an accelerated label approval process to manage the transition to 2D barcoding: Once manufacturers decide to begin implementing 2D barcodes on secondary packaging, they will need to get approval from the FDA for all label, product line, and software changes. FDA approval can take varied amounts of time depending on the variety of changes and the time of submission (e.g., annual process, ad hoc request). It is important to note that as the industry seeks to convert its artwork within the next two years, the FDA could be backlogged with approval requests that could further delay implementation timelines.

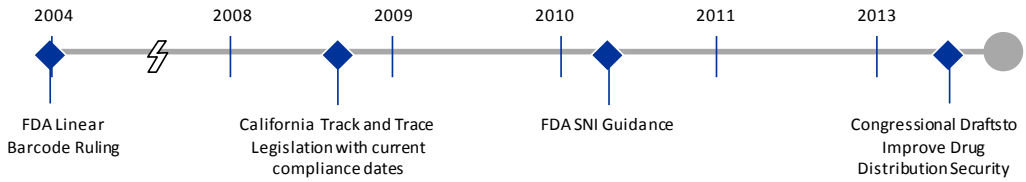
5 Appendices

5.1 Appendix A: Regulatory and Legislative Landscape

Evolving national standards regarding drug distribution security have created an emphasis on secondary packaging within the prescription drug industry. Regulatory and legislative actions have encouraged changes to data carriers on product packaging by proposing new data requirements that support increased supply chain visibility of drug products, including vaccines. In some cases, maintaining detailed transactional histories for the distribution of prescription drug products (i.e., product e-pedigrees) will be required as new laws take effect. There is increasing pressure on all supply chain participants to track, manage, and maintain more product-related information than ever before, which will require increased data capacity for data carriers used in the vaccine industry.

Since 2004, there have been several key pieces of legislation put into effect to increase drug distribution security and expand drug product information requirements. These are displayed in Figure 1.

Figure 1: Timeline of Recent Regulatory Actions



The 2004 FDA Linear Barcode Ruling[13] established linear barcodes as the industry standard for both primary and secondary packaging. Since then, the FDA has allowed vaccine manufacturers to file applications to add 2D barcodes to packaging. Moreover, track and trace (TnT) regulations and the adoption of serialization standards have been two additional drivers for shifting away from linear barcodes on vaccine packaging.

5.1.1 Current Data Carrier Requirements

In 2004, the FDA, in coordination with the U.S. Department of Health and Human Services (HHS), provided guidance requiring that prescription drugs' primary and secondary packaging include linear barcoding.[14] In 2011, however, the FDA adopted procedures for vaccine manufacturers to opt out of the linear barcode requirements for vaccine primary and secondary packaging since use of alternative technology "may enhance health care providers' ability to keep records and report adverse events."[15] FDA provides vaccine manufacturers the opportunity to request exemptions that allow for 2D barcodes either in place of, or in addition to, the linear barcodes. Therefore, it seems that the principle requirement adopted by the FDA is that the data carrier be uniform across a product line.

A gradual shift away from linear barcode requirements is already underway in primary packaging for vaccines. In early 2012, CDC launched a pilot program "designed to evaluate

[13] U.S. Department of Health and Human Services. "21 CFR Parts 201, 606, Et Al. Bar Code Label Requirements for Human Drug Products and Biological Products; Final Rule." U.S. Food and Drug Administration, 26 Feb. 2004. Web. <http://www.fda.gov/downloads/BiologicsBloodVaccines/DevelopmentApprovalProcess/AdvertisingLabelingPromotionalMaterials/BarCodeLabelRequirements/UCM154325.pdf>.
[14] "21 CFR Parts 201, 606, Et Al. Bar Code Label Requirements for Human Drug Products and Biological Products; Final Rule."
[15] Deloitte Consulting, LLP. "Two-Dimensional (2D) Vaccine Barcoding Manufacturers Forum Report." Centers for Disease Control and Prevention, 29 Feb. 2012. Web. <http://2dbarcodepilot.com/docs/Manufacturers_Forum_Report_FINAL.pdf>.

how 2D vaccine barcodes" on primary packaging "may affect the quality, accuracy, and timeliness of the exchange of immunization-related information."[16] Additionally, conversations with leading manufacturers, including many outside of the CDC pilot program, indicated that several of these manufacturers have held internal discussions and developed plans to adopt 2D barcode technology in the next three years.

5.1.2 Serialization

A key factor in the potential shift away from linear barcode technology is the development of supply chain standards for package-level serialization. In March 2010, the FDA provided industry guidance regarding standardized numerical identification (SNI) for prescription drug packages, which advanced a serialized national drug code (sNDC) for all prescription drug packages.[17] This code can include no more than 20 numeric and/or alphanumeric characters, and will help to enable national track and trace efforts. An impact of this serialization movement, however, has been an increase in the size of linear barcodes due to the additional characters.

The scope of FDA's guidance was limited to the

> "…smallest unit placed into interstate commerce by the manufacturer or the repackager that is intended by that manufacturer or repackager… for individual sale to the pharmacy or other dispenser of the drug product."

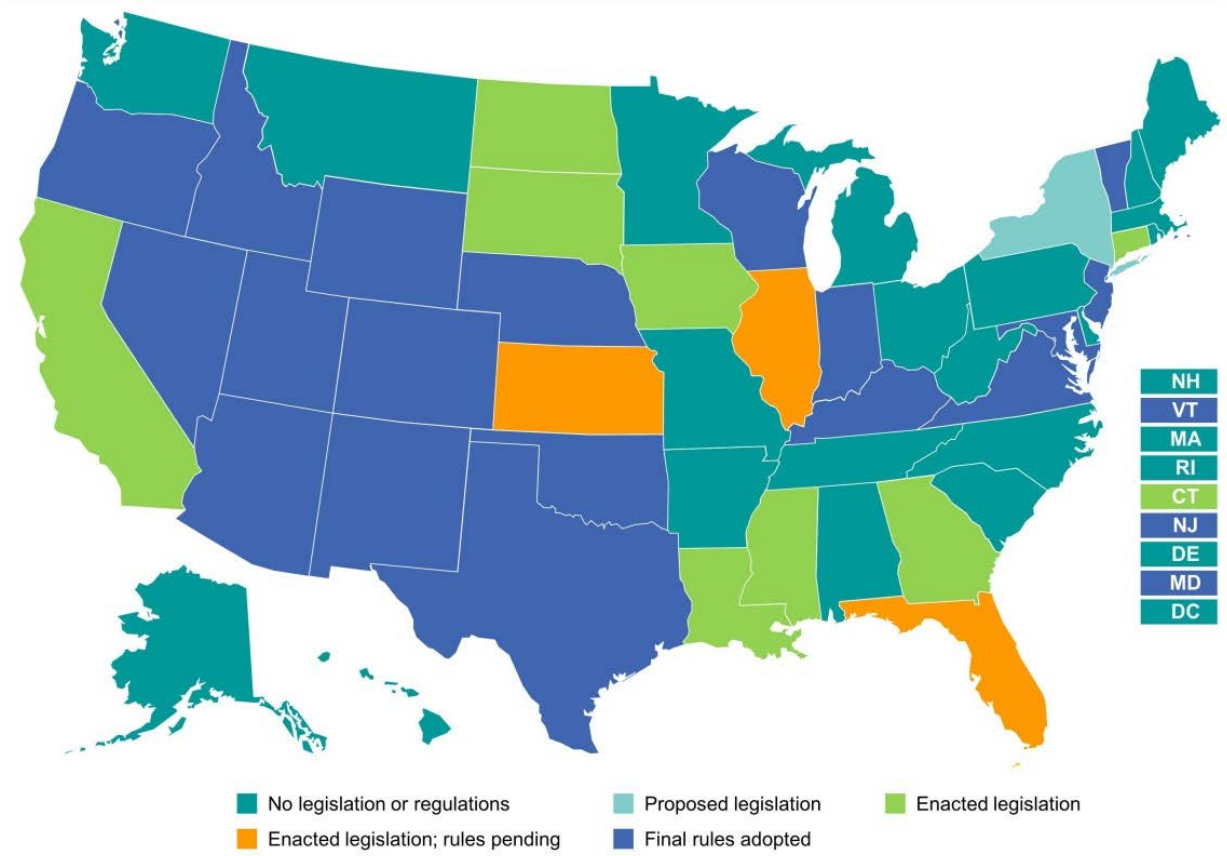
In other words, FDA's guidance is specifically related to saleable level packaging, which as discussed is actually secondary packaging for vaccines. The addition of a sNDC in an elongated linear barcode on secondary packaging is not as much of a space constraint as it is for primary packaging. It is, however, an issue of consistency and reliability. Increased linear barcode length could cause decreased accuracy in the scanning process, which in turn could reduce overall data reliability. To ensure the greatest possible accuracy, the external data carrier must facilitate simple and repeatable scanning.

5.1.3 Track and Trace

Prescription drug manufacturers have limited visibility into where their products might ultimately be dispensed. This creates obvious logistical compliance complications regarding identifying the specific state rules for each batch of product. Additionally, the variability and complexity of data requirements associated with tracking and managing differing state requirements makes the prospect of a patchwork solution daunting. Prior to DSCSA, states took varying approaches to track and trace requirements, with varying degrees of e-pedigree-related legislation and regulations (Figure 2). Direction provided by DSCSA standardizes track and trace requirements and timelines. This federalized approach should work to ensure track and trace capabilities are established regardless of state by November 2020.

[16] "Two-Dimensional (2D) Vaccine Barcoding Manufacturers Forum Report."
[17] U.S. Department of Health and Human Services. "Standards for Securing the Drug Supply Chain - Standardized Numerical Identification for Prescription Drug Packages." U.S. Food and Drug Administration, Mar. 2010. Web. <http://www.fda.gov/RegulatoryInformation/Guidances/ucm125505.htm>.

Figure 2: Overview of State Pedigree Legislation/Regulations

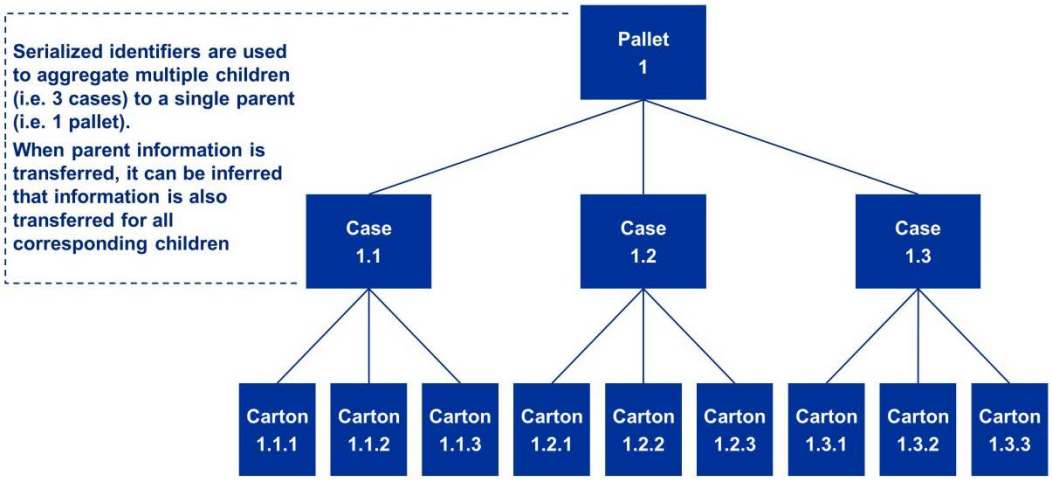


Source: Healthcare Distribution Management Association. "Distributor Licensing and Pedigree Requirements by State." Healthcare Distribution Management Association, 21 Jun. 2012. Web. <http://www.healthcaredistribution.org/gov_affairs/.state/state_legis-static.asp>.

In 2008, the state of California passed the most comprehensive of these requirements by enacting legislation requiring that by as early as 2015, saleable level prescription drugs be serialized and accompanied by electronic e-pedigrees. Since the enactment of this legislation, the U.S. Senate has made repeated attempts to propose federal requirements to relieve the drug supply chain from complying to patchwork solutions comprised of statutory requirements of varying complexity that differ by state.

DSCSA provides guidance toward a shared result: saleable level tracking and tracing for prescription drugs. A key component of any future shift toward saleable level e-pedigrees will be the ability to use aggregation and inference at a group-level in order to track product information (see Figure 3). This involves using aggregated e-pedigrees at the group level to infer the same transactional information for individual within-group units through parent-child relationships. Inference requires using external packaging data carriers to track group product information to the individual products themselves. As such, aggregation and inference requires that secondary packaging data carriers have a unique serialized number. Given that any future data carrier used on a product will need to have sufficient data storage capacity, it is likely that secondary packaging data carriers will play an increasingly prominent role in tracking detailed product information. Ideally, the future standard of data carriers should also support a simple, repeatable scanning process that helps ensure data integrity.

Figure 3: Parent-Child Relationship Diagram



Track and trace legislation plays an increasingly central role in promoting a shift away from linear barcodes. Specific track and trace requirements will rely heavily on the use of serialized product identifiers, which are easily implemented using modern data carriers such as 2D barcodes.

5.1.3.1 California's E-Pedigree Legislation

California's e-pedigree legislation introduced a comprehensive, interoperable electronic e-pedigree (e-pedigree) system across the supply chain for "dangerous" drugs, a classification that includes vaccines. The e-pedigree system, planned for a phased implementation across multiple years (Table 1), was superseded by DSCSA.

Table 1: California E-Pedigree Implementation Timeline

Date	Supply Chain Segment
January 1, 2015	**Manufacturers must serialize at least 50% of their prescription drug products and transmit/store valid e-pedigrees for all products sold or received.**
January 1, 2016	**Manufacturers must serialize all remaining prescription drug products.**
July 1, 2016	**Distributors and repackagers must receive, update, and transmit e-pedigrees for all prescription drug products received and sold. Repackagers must support serialized information, and link incoming serialized numbers to outgoing serialized package numbers.**
July 1, 2017	**Providers must receive and update e-pedigrees for prescription drug products. Drug packages, when returned, must be serialized.**

Source: California State Board of Pharmacy. "Board of Pharmacy - Information on E-Pedigree." *Board of Pharmacy - Information on E-Pedigree*. State of California, n.d. Web. <http://www.pharmacy.ca.gov/about/ e-pedigree_laws.shtml>.

As part of California's 2008 e-pedigree legislation, product transaction information would be maintained "…at the smallest package or immediate container distributed by the manufacturer, received and distributed by the wholesaler, and received by the

pharmacy or another person furnishing, administering, or dispensing the dangerous drug."[18]

In other words, the information would be tracked at the smallest unit of sale. According to the FDA's definitions for packaging, the smallest unit of sale may be at either the primary or the secondary packaging level. For all of the vaccine manufacturers included in this research, the smallest unit of sale is the secondary packaging level (Table 2).

Table 2: Examples of Lowest Saleable Vaccine Units

Vaccines[1]	Novartis	Merck	Sanofi	GlaxoSmithKline	MedImmune	Pfizer
Product Name	Fluvirin	Gardasil	PentACT-HIB	Pediarix	Flumist	Prevnar 13
Product Packaging						
Presentation and Packaging	Fluvirin is packaged in a 5-mL multi-dose vial	Gardasil comes in a carton of one 0.5-mL single-dose vial	PentACT-HIB comes with 1 Vial + 0.5mL syringe	Single-dose prefilled syringes containing a 0.5-mL suspension for injection	Package of 10 pre-filled, single-dose (0.2 mL) intranasal sprayers	Single-dose, prefilled syringe
Primary Packaging	Multi-Dose Vial	Syringe	Syringe	Syringe	Intranasal Spray	Syringe
Secondary Packaging	Carton	Carton	Carton	Carton	Carton	Carton
Lowest Saleable Unit	Secondary Packaging	Secondary Packaging	Secondary Packaging	Secondary Packaging	Secondary Packaging	Secondary Packaging

[1] Vaccines selected using 20 Top Selling Vaccines report (http://www.fiercevaccines.com/special-report/20-top-selling-vaccines/2012-09-25). Novartis top selling vaccine was unidentified and Fluvirin was selected as Novartis vaccine for analysis.

Secondary packaging is not always defined consistently. In the case of vaccines which combine multiple vaccines into a single shot, there may be multiple components packaged together for the administration of a vaccine (e.g., syringe, diluent, active ingredient). While each of these components has individual primary packaging, they are often sold together in a single carton. In such cases, the secondary packaging (i.e., the carton) is the saleable level unit that must carry the serialization information. Some vaccine products may also be sold in set quantities, with multiple vials or syringes included inside of a single box or carton. In such a scenario, the secondary packaging label (i.e., the label on the external box or carton) serves as the primary source of e-pedigree information.

To enable the traceability and passing of e-pedigrees for drug products destined for California, supply chain participants would likely leverage parent-child relationships within their packaging hierarchies, allowing for the tracking of multiple product e-pedigrees (i.e., an example of aggregation and inference, as discussed earlier). Although the manufacturer must initiate and e-pedigree, downstream supply chain partners need to "infer" child e-pedigrees through receipt of the parent e-pedigree. Inference enables process efficiencies, greatly mitigating the effort and costs associated with maintaining and appending product e-pedigrees. Inference, however, also creates the additional need for uniform, serialized external data carriers on vaccine secondary packaging (since individual packages must be identifiable in order to track specific hierarchical relationships). 2D barcode technology addresses this complexity. While not

[18] "Board of Pharmacy - Information on E-Pedigree."

necessarily the lone solution to these challenges, 2D barcoding is one viable alternative for providing the required capacity for an external data carrier.

The California legislation also required that "interoperable electronic systems" be established for the tracking, passing, and management of e-pedigree information across the supply chain. The California legislation, however, did not explicitly identify how e-pedigree information is to be stored or exchanged. An interoperable system could be either centralized or decentralized, with associated impacts to the broader supply chain resulting for each option. A centralized system requires information to be uploaded by different supply chain participants in a standard format to a publicly or privately hosted database, which would store both transaction histories and product information. Under this centralized approach, the use of standard formats would be an essential prerequisite to help ensure the system's overall functionality.

Under a decentralized scenario, information would not need to be stored in consistent formats, but would need to be compatible with selected user interfaces to ensure compatibility with both upstream and downstream supply chain partners. Failure to establish industry standards with respect to how information is recorded and transmitted would result in inherent inefficiencies and error. Industry stakeholders are therefore incentivized to establish and adopt standard data carriers and processes. 2D barcodes have the capacity and functionality to meet all the requirements of the California legislation and may very well serve as that standard data carrier.

5.1.3.2 DSCSA Origin

Federal lawmakers and regulators passed national standards for drug distribution security as the DSCSA to address the concern that the absence of national consensus might result in a problematic, patchwork solution in which vaccine supply chain participants would need to adhere to a plethora of different regulations across each state.

The U.S. Senate initially drafted legislation that preempted California's e-pedigree legislation. Their October 2012 provided broad guidance for implementing national standards for prescription drug safety.

A key distinction between California's e-pedigree legislation and the Senate legislation is that DSCSA allowed information transmission in either electronic or paper form. Additionally, and perhaps more importantly, the DSCSA only requires lot-level product tracking as opposed to saleable level. Overall, the DSCSA did not drastically alter the form of the e-pedigree system suggested by California.

5.2 Appendix B: Secondary Packaging Data Carriers Overview

Linear barcodes have been established as the industry standard for vaccine packaging since 2004. FDA guidance on the subject states:

> "The Agency intends for bar codes to be on the drug's outside container or wrapper as well as on the immediate container, unless the bar code is readily visible and machine-readable through the outside container or wrapper."[19]

Based on this guidance, linear barcodes are required on both primary and secondary vaccine packaging. In addition to the machine readable linear barcode requirement, the 2004 linear barcode ruling requires that critical human-readable information be placed on secondary packaging for prescription drugs and vaccines. An excerpt from the ruling states:

> "…the package of a biological product [will] be marked with the product's proper name, the name, address, and applicable license number of the product's manufacturer, and the product's expiration date… because the rule does not require lot number and expiration date information to be encoded, we decline to allow firms to remove the human-readable lot number and expiration date information from the label."[20]

As a result, all vaccines are now required to include lot number, expiration date, manufacturer name, and product name in human-readable form.

In light of shifting requirements for data carriers resulting from recent and proposed regulations, the prescription drug industry has been forced to recognize several core limitations of linear barcodes. As a result, the industry has become increasingly receptive to entertaining alternative data carrier technologies.

5.2.1 Limitations of Linear Barcodes

At the time of their introduction, linear barcodes represented a major step toward enhancing accuracy and efficiency throughout commercial product supply chains. Since that time, many advances in Automatic Information Data Capture (AIDC) technologies have emerged. When compared to other AIDC technologies, it is clear that linear barcodes have several limitations. This, coupled with federal and state guidance and legislation promoting track and trace and serialization, has increasingly pushed the industry toward considering alternative data carrier technologies such as 2D barcoding.

A major challenge associated with linear barcodes is that, due to the encoding methodology, they are not a space-efficient labeling technology. Linear barcodes, which consist of parallel lines, are only able to encode data in one dimension, resulting in a direct correlation between the amount of information encoded and the length of the barcode. Simply, the more information and characters included in the coding, the longer the physical length of the barcode will be.

The space requirements associated with linear barcodes pose challenges in meeting serialization requirements for upcoming legislation. As previously discussed, a sNDC would add the serialized product identifier to the current product national drug code (NDC). The most widely used linear barcode encoding format, the GS1 UPC-A linear barcode format, is limited to carrying 12 numerical digits.[21] As a result, the addition of a serial identifier would require

[19] U.S. Department of Health and Human Services. "Guidance for Industry: Bar Code Label Requirements—Questions and Answers." U.S. Food and Drug Administration, 11 Aug. 2011. Web. <http://www.gpo.gov/fdsys/pkg/FR-2011-08-11/pdf/2011-20385.pdf>.
[20] "21 CFR Parts 201, 606, Et Al. Bar Code Label Requirements for Human Drug Products and Biological Products; Final Rule."
[21] GS1. "Bar Code Types." GS1, n.d. Web. <http://www.gs1.org/barcodes/technical/bar_code_types>.

changes to the currently used data carrier standard and involve a transition to a different GS1 linear barcoding symbology capable of supporting additional characters.

Figures 4 and 5 depict two linear barcodes. The first image is of the traditional linear barcode with 12 numeric characters, which is roughly the amount of digits currently encoded. Figure 5 displays a more complex linear barcode that is encoded with 44 characters. These images clearly demonstrate how encoding additional data into a linear barcode impacts barcode lengths.

Figure 4: UPC-A Barcode

Source: GS1. "Bar Code Types." GS1, n.d. Web. <http://www.gs1.org/barcodes/technical/bar_code_types>.

Figure 5: Serialized Linear Barcode

Source: GS1 US. "GS1-128." GS1 US, n.d. Web. <http://www.gs1us.org/resources/standards/gs1-128>.

There are two main challenges with the use of elongated linear barcodes on secondary packaging. The primary issue is that the barcodes must be able to physically fit on vaccine secondary packaging. Although space concerns are more significant for primary packaging, it is also an important consideration for secondary packaging. The second issue is that as the barcode increases in size, it becomes challenging for barcode scanners to consistently read the data encoded. Even if linear barcodes can encode serialized information, if scanners are unable to accurately read the elongated barcodes during the scanning process, the entire symbology and information included in it are rendered useless.

Length limitations are a key reason why linear barcodes currently store only a product's NDC. As a result, additional important vaccine information (e.g., lot number, expiration date) is not currently encoded in the barcode of many products. It is typically presented, instead, in a human-readable format on secondary packaging. Since this additional product information is not readable via an AIDC technology, the data cannot be auto-populated in information management systems. In such cases, it must be manually entered if it is to be used at all. Such manual entry processes are time-consuming, and raise accuracy concerns due to potential human transcription error.

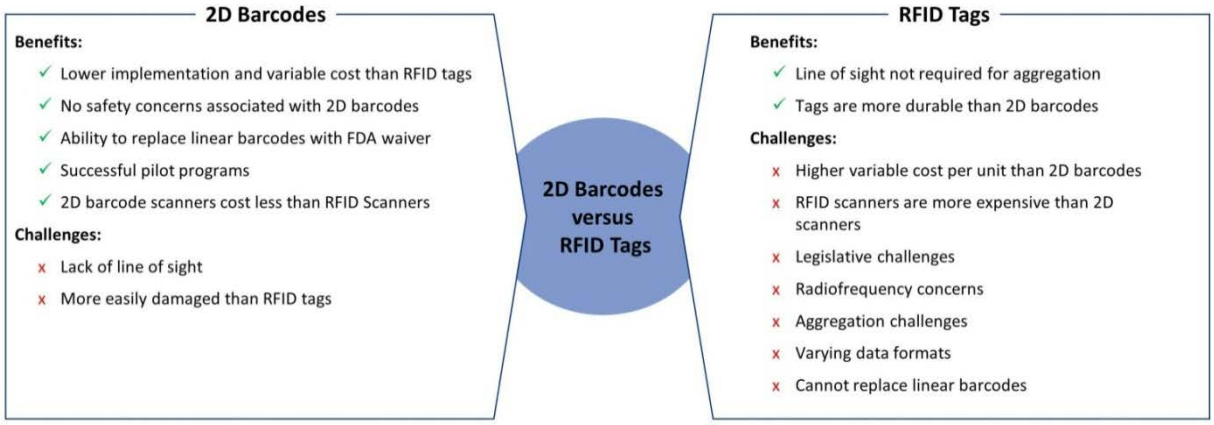
While theoretically capable of including serialized product information, size and consistency concerns pose clear logistical challenges that render linear barcodes ineffective solutions when compared to other AIDC technologies. For the industry to efficiently comply with

forthcoming legislative requirements, maximize the potential benefits offered by AIDC technologies, and further secure the U.S. drug distribution supply chain, a shift away from linear barcodes is needed.

5.2.2 2D Barcodes versus RFID

The limitations of linear barcodes demonstrate the need to adopt a modern AIDC technology capable of effectively meeting regulatory requirements. Based on the number of pilot projects across the industry, 2D barcodes and RFID tags are viewed as the most viable AIDC technologies, with each offering many benefits and additional capabilities when compared with linear barcodes. Key benefits derived from both 2D barcodes and RFID tags include: increased data storage capacity, space efficiency gains, and regulatory compliance. RFID and 2D can also be considered complementary technologies. If RFID were used as the primary carrier on a product, the 2D barcode could also be used as a back-up in the event a customer does not have RFID scanning capabilities. Figure 6 provides a comparison between 2D barcodes and RFID tags, highlighting the strengths and weaknesses of each technology compared to each other.

Figure 6: 2D Barcodes versus RFID Tags



Although both AIDC technologies offer significant improvements over linear barcodes, they have vast differences in terms of implementation and operational compatibility. Differences include cost, safety, and regulatory concerns, saleable level tracking implications, and industry consensus, among others. In addition, RFID can create some challenges with aggregation since RF units all boxed in together can create signal interference,[22] thus driving an inaccurate count. Orientation of cases on pallets can alleviate this issue, but it remains a challenge.

5.2.2.1 Cost

When comparing 2D barcodes and RFID tags, a key consideration for supply chain members is the implementation costs associated with each technology. While both technologies require sizeable initial capital investments, 2D barcodes offer cost savings relative to RFID tags in terms of variable and scanning costs. The variable per unit production cost of RFID tags has decreased in recent years; however, basic passive tags (the kind generally used for commercial

22 http://search.yahoo.com/r/_ylt=A0oG7hIfLoxRdl0ARU9XNyoA;_ylu=X3oDMTE1bTI0bDBkBHNlYwNzcgRwb3MDMwRjb2xvA2FjMgR2dGlkA1ZJUDIzN18xNzE-/SIG=12of4jole/EXP=1368170143/**http%3a//www.ti.com/rfid/docs/manuals/whtPapers/wp-SKU_Performance.pdf

products) still cost 7 to 15 cents each to produce. This is a substantial cost when compared to the relatively low cost of linear and 2D barcode printing.[23]

Although expensive on a per unit basis, increased storage capacity and product durability of RFID tags justify the higher cost in other industries. While RFID tags have increased storage capacity compared to 2D barcoding, such increased capacity is not required or necessary to meet current regulatory requirements for vaccines. Additionally, while RFID tags are very durable, and can be re-programmed and reused (thereby driving down the cost per use), the pharmaceutical supply chain is unable to avail itself of this RFID benefit. Given the complexities of the supply chain process and the amount of product produced on an annual basis by large manufacturers, it is impractical for manufacturers to expect RFID tags to be returned from downstream supply chain partners. The variable cost per tag, therefore, begins to increase; ultimately making RFID tags a costly option. Although not as durable as RFID tags, 2D barcodes can be simply affixed on secondary packaging in a cost-efficient manner. As a result, the variable cost per unit is much lower for 2D barcodes than for RFID tags.

Another important cost consideration involves the scanners necessary to use the different technologies. Based on our industry interviews, it appears that 2D scanners have become increasingly affordable in recent years, and are now comparable to linear barcode scanners in price. 2D scanner costs range from $300 to $350. In comparison, RFID scanners are much more costly, with the price per scanner ranging to upwards of $1,000.[23]

5.2.2.2 Safety and Regulatory Concerns

Since RFID tags have emerged as an alternative data carrier solution, pharmaceutical manufacturers have been concerned about the impact of the radio frequency (RF) signals these devices emit. These concerns stem from the potential impact that the RF thermal waves can have on the temperature of biopharmaceutical drugs. Research conducted to date indicates that these slight temperature changes have no impact on the active ingredients in different vaccines.[24] While RFID technology appears safe for biopharmaceutical products, there remain certain restrictions on the use of RFID technology for vaccines.

FDA Compliance Guideline 400.210 has specific criteria under which RFID tags may be used in testing scenarios. [25] These use restrictions create challenges and regulatory hurdles for supply chain members interested in running pilot programs to evaluate the effectiveness and safety of RFID technology.[26]

Based on industry research and interviews, there appear to be few concerns reported involving patient safety and 2D barcodes. Additionally, 2D barcodes are permitted to be used on biopharmaceutical drugs, alleviating regulatory concerns in that regard. As a result, industry members have been able to conduct pilot tests for 2D barcode technology, which have both helped validate the technology's effectiveness and increase industry familiarity with it.

Regulations state that RFID tags are currently unacceptable as replacements for linear barcodes, and can only be included as supplementary information carriers on vaccine secondary packaging. This means that manufacturers who add RFID tags to secondary packaging would be required to include both RFID tags and the linear barcodes on vaccine

23 RFID Journal. "Frequently Asked Questions." RFID Journal, n.d. Web. <http://www.rfidjournal.com/faq/20>.
24 http://www.pharmamanufacturing.com/articles/2011/088.html?page=print#
25 U.S. Department of Health and Human Services. "CPG Sec. 400.210, Radiofrequency Identification Feasibility Studies and Pilot Programs for Drugs." U.S. Food and Drug Administration, 28 June 2011. Web. <http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074357.htm>.
26 Uysal, Ismail. RFID and Biologics. N.p.: USP Workshop on Supply Chain Integrity, n.d. PDF.

secondary packaging. For 2D barcodes, the FDA has instigated a waiver process by which manufacturers can entirely replace linear barcodes with 2D barcodes for vaccine products.[27]

5.2.2.3 Saleable Level Tracking Implications

One of the key benefits of using RFID tags is that they do not require line of sight for scanning, which means that you do not have to be able to physically see the RFID tags while scanning items within a box. Theoretically, this means that multiple, individual products within a box can be easily scanned; thereby limiting the amount of labor time spent manually scanning. This would improve the efficiency of aggregation within the distribution process (once regulations are implemented). The limited testing of RFID technology, however, has shown instances where multiple tags stacked closely together have interfered with each other's signals, resulting in incorrect scans.[28] In other cases, incomplete scans occurred, resulting in not all of the products within a box being properly identified (unbeknownst to the supply chain participants performing the scans). Such limitations, therefore, may limit the feasibility of using RFID tags for saleable level tracking.

2D barcodes, by comparison, do require line of sight, meaning that they must be visible in order to be scanned. As a result, product information needs to be aggregated based on product hierarchies in order to avoid breaking apart shipments to scan all individual units when regulations take effect. This process of inference inherently requires trust between supply chain partners and creates the potential for inaccuracies insofar should product hierarchies be improperly maintained.

Irrespective of technology, tracking and tracing of products will create challenges throughout the supply chain. Neither alternative represents an ideal solution, but at present 2D barcodes offer a more consistent solution to track transaction information at a saleable level.

5.2.2.4 Industry Consensus on data formats and use

While not perfect, the cost advantages, familiarity, and reduced regulatory hurdles associated with 2D barcodes have made them the industry preference as an alternative data carrier. RFID tags surpass 2D barcodes in terms of durability and information storage capacity, but these advantages are mitigated by cost, safety, and other functionality concerns. There is also continued discussion regarding the formatting of data when using RFID tags. Because of the increased data capacity, it is inviting to add more data than required to enhance value and that data may not be aligned to a standard that exists.

5.2.3 2D Barcodes Encoding Characteristics

2D barcodes store information by encoding data both horizontally and vertically. There are many different variations of 2D barcodes, but GS1 standards have largely focused on the Data Matrix Error Correction Code (ECC) 200 barcode, thereby making it the most widely used 2D barcode format within the prescription drug industry.

Along with the benefits already mentioned, 2D barcodes offer solutions to many linear barcode limitations. They have the potential to provide increased data storage capacity, enhanced accuracy, reduced errors, space efficiency gains, and enable regulatory compliance. Data Matrix barcodes can either be square or rectangular. The more commonly used square

[27] U.S. Department of Health and Human Services. "Federal Register, Volume 76 Issue 155 (Thursday, August 11, 2011)." U.S. Food and Drug Administration, 11 Aug. 2011. Web. <http://www.gpo.gov/fdsys/pkg/FR-2011-08-11/html/2011-20385.htm>.

[28] http://search.yahoo.com/r/_ylt=A0oG7hIfLoxRdl0ARU9XNyoA;_ylu=X3oDMTE1bTI0bDBkBHNlYwNzcgRwb3MDMwRjb2xvA2FjMgR2dGlkA1ZJUDIzN18xNzE-/SIG=12of4jole/EXP=1368170143/**http%3a//www.ti.com/rfid/docs/manuals/whtPapers/wp-SKU_Performance.pdf

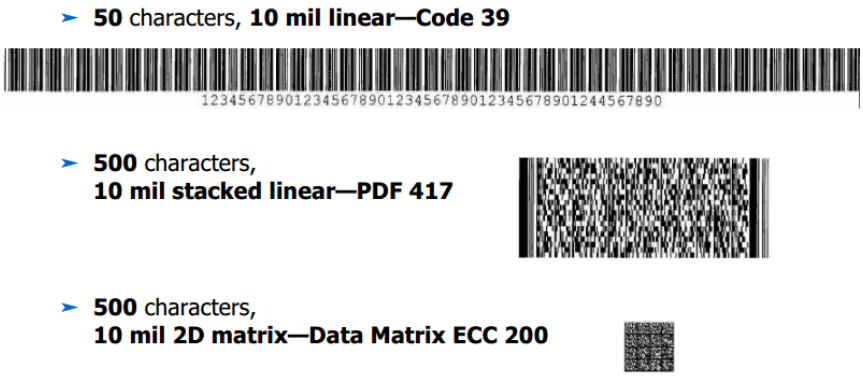
barcodes are capable of encoding more information; however, the rectangular barcodes allow for higher-speed printing of the barcode on the production line (Figure 7).[29]

One of the main benefits associated with 2D barcodes, as compared to linear barcodes, is their ability to encode substantially more information in a much smaller space. This allows for product serialization, improves accuracy and efficiency of scanning through consistency in the size of the barcode, and addresses packaging space concerns. Figure 10 illustrates the ability of a Data Matrix barcode to store significantly more characters in a much smaller amount of space than a standard, or even a stacked, linear barcode.

Figure 9: Square and Rectangular Data Matrix Barcodes

Source: GS1. "GS1 DataMatrix." GS1, n.d. Web.
http://www.gs1.org/docs/barcodes/GS1_DataMatrix_Introduction_and_technical_overview.pdf

Figure 10: Comparison of 1D Linear, Stacked Linear and 2D Data Matrix

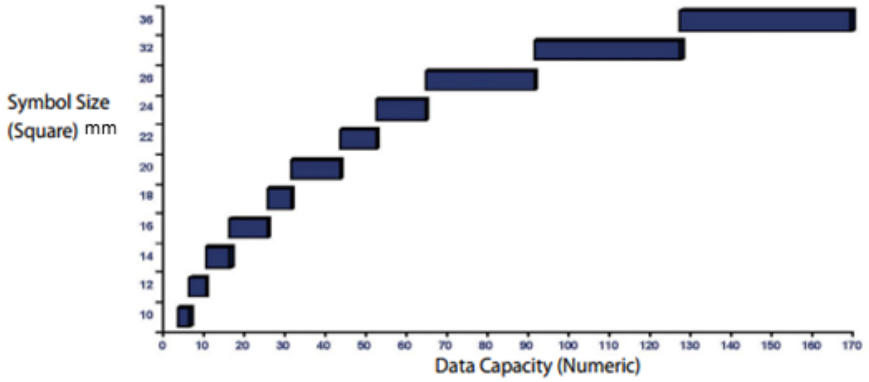


Source: Microscan. "About Data Matrix Symbology." Microscan, n.d. Web. <http://www.barcode-fonts.de/microscan/DataMatrix_Code.pdf>.

Figure 10 offers a powerful demonstration of the space-saving capability offered by Data Matrix barcodes, as the Data Matrix barcode stores 10 times more product information than a linear barcode and does so in less than one-tenth the space. Figure 9 demonstrates the correlation between symbol size and data capacity for a Data Matrix barcode. Minimal increases in the size of the Data Matrix barcode result in a substantial increase in its data storage capacity.

Figure 11: Data Matrix Storage Capacity

[29] GS1. "GS1 DataMatrix." GS1, n.d. Web. <http://www.gs1.org/docs/barcodes/GS1_DataMatrix_Introduction_and_technical_overview.pdf>.



*** Exact size of the Data Matrix symbol depends on the exact encoded data**

Source: GS1. "GS1 DataMatrix." GS1, n.d. Web. <http://www.gs1.org/docs/barcodes/GS1_DataMatrix_Introduction_and_technical_overview.pdf>.

5.2.3.1 Error Correction

Another major benefit provided by the Data Matrix ECC 200 technology is that it includes error correction functionality. According to the GS1 Data Matrix overview:

> "The Reed-Solomon error correction calculates complementary codes and add-ins during the creation of the symbol, [and] reconstitutes the original encoded data by recalculating the data from the complementary codes and add-ins. The recalculation regenerates the original data by locating errors at the time of scanning. Such errors may be the result of printing problems, specular reflection, or degradation of the printed surface."[30]

This error correction technology represents a key benefit in the industry's push towards 2D barcode technology. It will potentially help to reduce process inefficiencies and miscommunications between supply chain members by both identifying data errors and helping to resolve them.

5.2.3.2 GS1 Standards

GS1 is a global, non-profit organization that helps to develop supply chain standards around the world. GS1 standards are the most widely used standards in the world, and as a result, they are generally followed by the pharmaceutical supply chain.[31] According to a 2012 survey, 55% of pharmaceutical manufacturers planned to use GS1 standards at the package level going forward.[32] The near universal adoption of GS1 standards means that any conversation about the adoption to of 2D barcodes must include discussion of the impact of GS1 standards on their implementation.

According to GS1 Standards, 2D barcode information must be encoded in the Data Matrix ECC 200 format.[33] This standard format is created to allow uniform data entry across the industry and to avoid process inefficiencies and miscommunications between supply chain partners. The quality of the 2D barcode images printed is extremely important for scanning purposes and coordination with downstream partners. Print quality is measured for symbols based on grade, aperture, light, and angle. The overall International Organization for Standardization (ISO) symbol grade is the most important factor in determining a symbol's print quality.[34]

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[30] "GS1 DataMatrix."
[31] GS1. "About Us." GS1, n.d. Web. <http://www.gs1.org/about>.
[32] Healthcare Packaging. *Pharmaceutical Track-And-Trace Serialization Playbook*. N.p.: Healthcare Packaging, 2013. PDF.
[33] "GS1 DataMatrix."
[34] International Organization for Standardization. International Organization for Standardization. ISO, n.d. Web. <http://www.iso.org/>.

5.3 Appendix C: Vaccine Supply Chain Overview

The global vaccine market has experienced rapid growth in recent years. Over an eight-year period from 2000 to 2008, industry-wide revenue nearly tripled to $17 billion. [35] The global market is forecasted to continue growing to approximately $25 billion in revenue by the year 2015.[36] Driving this growth over the last decade has been the development of many groundbreaking and potentially life-saving vaccines.[37] In total, the industry now produces over 600 vaccine products.[38]

The global market for manufacturers is relatively crowded with 200 to 250 different companies operating across the globe. Competition has intensified due to the entry of several new biotech and pharmaceutical companies into the market. Despite the intense competition in the industry, however, the majority of sales continue to be centralized around a few large companies with long-term expertise, research and development capabilities, and patents in the vaccine field.[39]

5.3.1 United States Vaccine Market Background

To better understand the implications of packaging changes on the vaccine supply chain, it is important to understand the composition of U.S. vaccine manufacturers and to understand the distinction between the public and private vaccine markets. While certain international regulatory trends may have an ancillary impact on packaging decisions by U.S. vaccine manufacturers, a detailed discussion of the international vaccine market is not included.

5.3.1.1 Background

The United States vaccine market is characterized by high immunization rates and the continuous launch of innovative, new vaccines to meet evolving public needs. Eleven manufacturers produce FDA-approved vaccines for the U.S. market, with the seven largest producers accounting for 90% of the total market.[40] Pediatrics represents the largest group of vaccine users, and pediatric demand is predictable, as it is directly correlated to the total births annually.[41]

As the U.S. population is projected to increase in the coming years, and the increase in elderly patients will peak, the pharmaceutical and vaccine markets are projected to grow as well. Unfortunately, the increased market size and potential has also provided increased opportunity for illicit activity due to rising prices and limited access. As a result, there have been increases in counterfeit and illegal drugs entering the global marketplace, thereby putting patient safety in question. While the drug supply chain in the U.S. remains among the most secure in the world, counterfeiting and patient safety concerns remain key drivers of regulations aiming to further strengthen security throughout the drug distribution process.

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[35] World Health Organization. "Vaccination: Rattling the Supply Chain." WHO, 2011. Web. <http://www.who.int/bulletin/volumes/89/5/11-030511/en/index.html>.
[36] PRWeb. "Global Human Vaccines Market to Reach US$25 Billion by 2015, According to a New Report by Global Industry Analysts, Inc." PRWeb, 11 Jan. 2011. Web. <http://www.prweb.com/releases/human_vaccines/prophylactic_therapeutic/prweb8055092.htm>.
[37] "Vaccination: Rattling the Supply Chain."
[38] "Global Human Vaccines Market to Reach US$25 Billion by 2015, According to a New Report by Global Industry Analysts, Inc."
[39] "Global Human Vaccines Market to Reach US$25 Billion by 2015, According to a New Report by Global Industry Analysts, Inc."
[40] RTI International. *Impact of a Two-Dimensional Barcode for Vaccine Production, Clinical Documentation, and Public Health Reporting and Tracking.* N.p.: Centers for Disease Control and Prevention, n.p., July 2012. PDF.
[41] *Impact of a Two-Dimensional Barcode for Vaccine Production, Clinical Documentation, and Public Health Reporting and Tracking.*

5.3.1.2 Private versus Public Vaccines

Globally, the largest purchasers of vaccine products are government agencies. This holds true in the United States as well. Government purchasing entities include federal programs and agencies such as the Vaccines for Children (VFC) program and the U.S. Department of Veteran's Affairs (VA). State and local governments also make purchases through public health departments, which administer vaccines at subsidized health clinics.

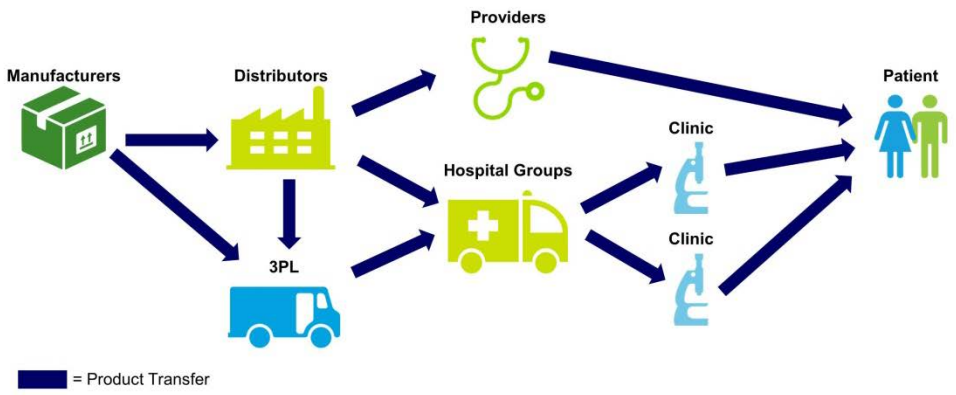
Public vaccine funding is predominantly allocated to underinsured or uninsured patients, including Medicaid- and Medicare-eligible patients. More specifically, these funds are generally allocated to pediatric patients in order to ensure nationwide vaccination against high-risk diseases. Many state immunization programs require providers to receive approval to administer publicly funded vaccines, and often require approved providers to separately track and report publicly funded vaccine inventories.

Privately purchased vaccines are paid for either by individual patients or through their insurance companies. While the prices of publicly purchased vaccines are negotiated by large governmental programs such as the VFC program, the prices of privately purchased vaccines are determined by market demand.

5.3.2 Key Supply Chain Members

The vaccine supply chain consists of combinations of seven key stakeholders, including manufacturers, distributors, third-party logistics providers (3PL), hospital groups, clinics, providers, and patients. Figure 10 depicts the relationships between supply chain partners as vaccine products flow from the manufacturer down to the patient. While not included in Figure 10, government agencies interact with varying components of the supply chain through either information or product transfers.

Figure 12: Simple Vaccine Supply Chain Outbound Logistics Overview



The role of the manufacturers in the supply chain consists of producing, packaging, and selling vaccine products. Once the vaccines are produced and packaged, they are generally sold to distributors. The distributors warehouse bulk quantities of different vaccines from myriad manufacturers. Distributors are then able to process orders from providers for multiple product types. These orders are filled typically through a "pick and pack" process from internal inventory stocks, and then distributed to downstream partners such as hospital groups and providers. Distributors may also, in certain instances, provide ancillary services such as product

repackaging. In this process, additional bundling or packaging of multiple products occurs at distributor warehouses, and then items are similarly sold and distributed downstream.

Many hospital groups leverage centralized purchasing departments in order to realize economies of scale. In their role as a group purchasing entity, hospital groups receive large shipments of vaccines and distribute smaller quantities to clinics and providers within their hospital network. Clinics and providers represent the interface with end-users (i.e., patients). This group includes state-funded clinics, private practices, and retail pharmacies and/or commercial vaccinators. Once they receive the vaccines, they then administer the vaccines to the patient and store necessary information within the patient's medical record and IIS.

The role of 3PLs within the distribution process varies depending on the manufacturer and distributor. 3PLs can provide basic distribution support in terms of transporting product from point to point, or can provide comprehensive logistics solutions and support for the manufacturer. Some manufacturers use dedicated 3PL teams in order to exclusively support their product distribution needs. Distributors may also contract 3PLs to provide ancillary logistical support as needed. 3PLs often play a significant role in receiving and processing returned products for manufacturers and sometimes distributors. In this reverse logistics role, 3PLs receive, process, and dispose of returned products for manufacturers and sometimes distributors. A key distinction for 3PLs is that, unlike distributors, they do not actually purchase or own the vaccines.

The VFC program operates as a group purchasing organization, whereby it negotiates favorable prices for pediatric vaccines on behalf of providers registered within the program. The VFC program purchases the vaccines but does not physically receive, store, distribute, or administer the vaccines. The VFC program also provides an online interface for registered providers to submit orders and track publicly purchased inventory. The VFC program outsources its logistics needs to third-party distributors.

For purposes of this report, stakeholders have been grouped into three distinct categories: manufacturers, distributors, and providers. Given their similarities, 3PLs have been included as part of distributors. Similarly, hospital groups, health clinics, public health departments, retail pharmacies, family physicians, and all other providers have been grouped together jointly as providers. While there may be certain unique impacts that are not shared across the entire group, they collectively provide a representative perspective of their position in the supply chain.

5.3.2.1 Manufacturers

Manufacturers play a critical role in the vaccine supply chain, as they produce the vaccines that are transported downstream and administered to patients. Manufacturers would likely be exposed to many of the challenges, process adjustments, and capital expenditures associated with any changes in industry standards.

The vaccine manufacturing industry is highly consolidated; therefore, technology adoptions made by these key stakeholders have significant influence in terms of industry standards and can often establish the generally accepted standard of care.

From a packaging perspective, manufacturers' ability to dictate how information is presented is restricted by regulatory and legislative standards. Human-readable content is required for vaccines on both primary and secondary packaging, and any meaningful changes to packaging artwork or the currently mandated linear barcodes must be submitted to and approved by the FDA. However, the new waiver process previously discussed provides vaccine manufacturers a choice in which data carrier to include on their vaccine packaging. After years of exclusively

using linear barcodes on vaccines, vaccine manufacturers have begun to provide products with 2D barcodes on the primary label.

In consideration of DSCSA requirements, many leading manufacturers have already established clear internal timelines for adopting 2D barcodes on the packaging of their vaccine products. As such, capital investments have either begun to be made, or will be made within the next twelve to eighteen months in order to enable 2D barcode printing functionality. As manufacturers continue to move towards adopting 2D capabilities, they are serving as the catalysts for change toward the broader adoption of 2D barcodes throughout the vaccine supply chain.

Leading manufacturers are making investments in 2D printing capabilities not only because of DSCSA, but also due to a global shift in international drug distribution standards. Remaining decisions on DSCSA will affect downstream use of 2D barcodes (i.e., whether or not they are used for aggregation or inference), but may not have a significant impact on the timeline for global manufacturers' implementation of 2D capabilities.

5.3.2.2 Distributors

Distributors play a significant role in the supply chain, as they consolidate industry demand and receive vaccines from manufacturers, in some cases repackaging the vaccines, and then transport them to other distributors or supply chain members further downstream. Since distributors work closely with manufacturers and providers, their adoption approach toward 2D barcodes on secondary packaging is heavily impacted and dependent on their upstream and downstream supply chain partners' strategies and capabilities.

Distribution of drug and vaccine products is a highly competitive, volume-based industry with margins as low as 3% in certain market segments, based on conversations with leading distributors and vaccine industry members. As a result, distributors are extremely cost-sensitive, and are not typically inclined to make significant shifts in infrastructure (unless business or regulatory requirements provide a need for change). Distributors, however, must respond to the needs of the market and their customers in order to remain competitive in the marketplace.

Distributors currently use linear barcodes on secondary packaging primarily for inventory management. Linear barcodes are scanned during the package receipt process, and information extrapolated from that barcode, typically product name and NDC code, are stored electronically within inventory management systems. Given that expiration date and lot number are not currently encoded within an AIDC for most vaccines, however, this information is not tracked as part of inventory management. As a result, product expiration and recall management are conducted through manual product checks and manual reports.

The distributors we interviewed for this study conveyed that, aside from pilot programs, they currently receive and scan very few prescription drug products containing 2D barcodes on secondary packaging. Given that nearly all drug products must contain linear barcodes, distributors' processes are designed to meet the demands of a largely linear-based industry. All of the distributors interviewed did, however, mention that they currently had 2D scanning capability, albeit with varying capacity constraints, at their distribution facilities.

Distributors indicated that many manufacturers are beginning to adopt 2D barcodes on their product lines, causing distributors to position themselves to adopt 2D barcode technology and capabilities to meet the future needs of their customers. In addition, DSCSA mandates that distributors enact lot-level traceability by November 2019, further promoting their adoption of 2D barcodes on secondary packaging in order to support product aggregation and inference.

However, distributors are able to continue to use linear barcodes at the pallet level as real estate on the pallet packaging allows for serialized linear barcodes.

Still, it appears distributors have yet to finalize implementation timeframes for the adoption of 2D barcodes on secondary packaging. The industry seems to be following the manufacturers' lead in the transition to 2D barcodes, with manufacturers' requirement to comply with DSCSA application of 2D barcodes by November 2017. Distributors also play a unique role within the supply chain as they can potentially provide repackaging services based on customer needs and their respective business model. When a distributor performs repackaging services, they essentially replicate the manufacturer's role in the supply chain as they print and place their own labeling on external packaging. As 2D barcodes appear increasingly likely to be the data carrier that the industry will adopt to meet e-pedigree requirements, repackagers may face similar pressures to those faced by manufacturers to adopt the technology as an industry standard.

5.3.2.3 Providers

Health care providers receive vaccines from upstream supply chain partners and administer the vaccines to patients. The inventory receipt process for vaccines varies slightly depending on the provider and the amount of information they wish to store. While providers may store differing information in their inventory management systems, all providers generally store the following in their EMRs: vaccine type, quantity, dosage, manufacturer name, product name, product NDC, lot number, and expiration date. Many hospital groups, some retail pharmacies, and certain larger health practices currently have linear scanners and are able to pull a portion of this information from barcodes on vaccine secondary packaging.

Currently, the information included within linear barcodes is limited to the NDC, which can be cross-referenced to obtain additional context such as product and manufacturer name. The balance of the information can be manually entered into their inventory management system either from the secondary packaging or from the shipment invoice, which is verified against the secondary packaging. This information is typically uploaded to the provider's EMR system, which then allows a physician to select the appropriate product information from a drop-down list when entering vaccination information into a patient's electronic medical record. For providers without scanning capabilities, all information is entered into inventory management and EMR systems manually.

Outside of the inventory receipt process, secondary packaging provides little utility for providers. While industry best practices call for vaccines to be stored within secondary packaging, a portion of providers discard secondary packaging upon receipt of a product and instead store the vaccine in its primary container (i.e., vial or syringe) in order to maximize refrigerator storage space. Once a vaccine is administered to a patient, providers are legally required to record key vaccine product information including lot number, product ID, expiration date, manufacturer, and product name. Most providers enter this information into the patient medical record based on the primary packaging, and not the secondary package. This occurs primarily due to the risk of incorrect information on the secondary packaging such as lot number or expiration date. This information can be entered manually, selected from pre-loaded drop-down lists, or scanned from the primary packaging. In any case, the secondary packaging is typically not used during this process.

Providers handle and administer both privately purchased and publicly subsidized vaccines. Certain public vaccine stocks require additional inventory reporting on data elements such as quantities, lot number and expiration dates, most of which is entered manually into online inventory tracking databases. IIS immunization registry reporting requirements vary by state.

The CDC IIS Recommended Core Data Elements lists the vaccine type and lot number as required fields. Vaccine expiration date is an optional reporting value.[42]

Aside from certain hospitals and large provider practices, most providers do not currently have 2D scanning capabilities, and many do not even have linear scanners. As part of the 2D vaccine barcode pilot project, more than 200 providers were selected to participate. Of these, only two had scanning capabilities, with one able to scan linear barcodes and the other able to scan 2D barcodes. Very few products currently received by providers, vaccine-related or otherwise, have 2D barcodes. As of August 2014, only 28 vaccine presentations have 2D barcodes applied to their secondary packaging. Furthermore, the information encoded in linear barcodes for vaccines typically includes only product NDC. As such, the bulk of data that need to be recorded from a package is being transmitted to providers in human-readable form. The limited usefulness of current linear barcodes and the limited quantity of 2D barcoded products have in many ways discouraged industry adoption of scanning technologies.

Providers have thus far made limited decisions with respect to technology upgrades to accommodate 2D barcodes, serialization, or e-pedigrees. DSCSA requires providers to have lot-level traceability by November 2019. This gives providers an ample amount of time to adjust processes and inventory management systems in order to be DSCSA compliant..

5.3.2.4 VFC Program

The Vaccines for Children (VFC) program is a federally funded initiative that strives to protect children by providing free vaccines to babies, young children, and adolescents who otherwise would be unable to afford them.

There are currently more than 44,000 doctors nationwide registered as VFC providers. Children are eligible for vaccinations from the VFC program if they are under the age of 19, and are either uninsured, underinsured, Medicaid-eligible, or American Indian or Alaskan Natives. The VFC program currently offers 16 vaccines to protect children, all recommended by the Advisory Committee on Immunization Practices (ACIP). The quantity of product purchased by the VFC means the program has broad influence within the industry, and potentially the ability to leverage its role to encourage adoption of new standards by manufacturers. [43]

The VFC program facilitates vaccine purchasing by negotiating discounted prices with select manufacturers and providing state awardees with access to a centralized purchasing system. Orders are placed by providers through immunization program awardees and fulfilled by its contracted distributor. Enrollment of individual providers is managed by immunization program awardees, typically state immunization boards. These awardees are also responsible for receiving immunization information from providers and projecting annual demand for planning purposes.

The VFC program negotiates multi-year contracts with vaccine manufacturers and distributors, which helps stabilize the price of VFC vaccines. As a result, the VFC program is not substantially impacted, either positively or negatively, by short-term price fluctuations. The VFC's main concern is the long-term trend in the price of vaccines.

The VFC program is aware of the industry movement toward 2D barcodes on secondary packaging, and is cognizant of the fact that the industry will be impacted by this transition. The VFC program is also in the process of implementing large-scale systems changes, as it attempts

[42] http://www.cdc.gov/vaccines/programs/iis/core-data-elements.html
[43] Centers for Disease Control and Prevention. "About VFC." Centers for Disease Control and Prevention, 31 Aug. 2012. Web. <http://www.cdc.gov/vaccines/programs/vfc/about/index.html>.

to streamline and improve its online ordering system. As a result, the VFC program will likely prioritize changes to its ordering system before shifting attention toward the challenges and benefits presented by 2D barcodes on vaccine secondary packaging.

5.4 Appendix D: Glossary

2D Barcode: Machine-readable graphical images that store data both horizontal and vertical dimensions

Aggregation: The process by which manufacturers pack their serialized unit products of drugs into serialized shipping cases

Automatic Identification and Data Capture (AIDC): AIDC technology encodes product data into a format that can be scanned and automatically entered into a computer system (e.g., barcodes, RFID)

Cold Chain: A cold chain is a temperature-controlled supply chain. It often is composed of a series of storage and distribution actions that are consistently performed at a given temperature range. Cold chain pharmaceuticals require this specific handling to ensure the efficacy of products and the specific temperature (and time at temperature) tolerances depend on the actual product being shipped. Maintaining a cold chain is critical in the vaccines market given that many vaccines may need to travel long distances in extreme climates to serve clinics and patients in countries with limited infrastructure.

Data Carrier: An AIDC technology capable of storing machine-readable data

E-pedigree: An electronic version of a pedigree

Electronic Medical Record (EMR): Electronic versions of patient medical records; these records store product information for vaccines administered to patients

eMAR: Electronic medication administration record (eMAR)

Expiration Date: The last date of effective use for a product, after which point in time the product must be disposed of

GS1: GS1 is a global, non-profit organization that helps to develop supply chain standards around the world

Immunization Information Systems (IIS): Per CDC, IIS are "confidential, population-based, computerized databases that record all immunization doses administered by participating providers to persons residing within a given geopolitical area"

Inference: The use of aggregated e-pedigrees at a group level in order to infer the same transactional information for individual units contained within the group through a parent-child relationship

Linear Barcode: One-dimensional barcodes that consist of parallel lines and spaces of various widths that create specific patterns that encode data

Lot Number: Number assigned to a specific subgrouping of products produced by a common manufacturer

National Drug Code (NDC): Per the FDA, NDC is "a unique, three-segment number… which serves as a universal product identifier for human drugs"

PMS: Practice Management Software

Parent-Child Relationship: Within the scope of aggregation, it is the relationship between a package (i.e., parent) and its components (i.e., children)

Pedigree or e-pedigree: A record, in paper (pedigree) or electronic (e-pedigree) form, which contains information for each change of ownership transaction

Prescription Drug: A drug that requires a doctor's authorization to purchase

Primary Packaging: Per the FDA, primary packaging is the "packaging component that is or may be in direct contact with the dosage form"

Radio Frequency Identification Device (RFID): A data carrier that utilizes electronic tags in order to store data

Secondary Packaging: Per the FDA, secondary packaging is the "packaging component that is not and will not be in direct contact with the dosage form"

Short Date: The practice of selling soon-to-expire products at a discount or prioritizing their sale to the immunization community to ensure the products are used in a timely manner

sNDC: A serialized NDC identifier for pharmaceutical products

Track and Trace: Standards for tracking and tracing a prescription drug through the supply chain from the point of manufacture to point of dispense

VFC:

Vaccine Tracking System (VTrckS): Per CDC, VTrckS "is an information technology system that integrates the entire publicly-funded vaccine supply chain from purchasing and ordering to distribution of the vaccine"

5.5 Appendix E: Sample Interview Questions

Manufacturers

1. Please describe your packaging hierarchy for the vaccines that you manufacture.

2. What do you consider the distinction to be between primary and secondary packaging (i.e., where in the hierarchy do you consider the exterior packaging to be secondary)?

3. Please explain your current labeling operations (i.e., how and where labels are affixed/imprinted onto secondary vaccine packaging). What is the product process flow following labeling?
    a. What current FDA requirements or industry consensus standards are currently followed by your firm for how information is presented on labeling? Do any of these regulations/standards conflict with potentially adding 2D barcoding?

4. How many secondary packaging lines do you currently operate for vaccines? Is there a proportionate amount of labeling systems to vaccine secondary packaging lines?

5. What specific data carrier do you currently use on vaccine secondary packaging (e.g., linear barcode, 2D barcode, RFID, text)?
    a. If currently using 2D barcodes as a data carrier:
        i. What symbology is used (e.g., Data Matrix, QR)?
        ii. Where is the data carrier located on the packaging?
    b. Please explain any plans to modify/add to your current vaccine secondary packaging data carrier.
    c. Are you planning on having multiple data carriers on a single package?
    d. How does your data carrier for vaccine secondary packaging relate to individual components for multi-component vaccines?

6. Do you use a data carrier on shipping invoices/manifests for vaccines?
    a. If not, what would be the challenges of incorporating a 2D barcode to your invoice/shipping manifest?

7. What vaccine products do you currently produce with 2D barcoding on secondary packaging?
    a. What is the degree of complexity, cost, or effort associated with printing 2D barcoding on secondary packaging for additional product lines?
    b. What is the additional effort/cost, if any, of printing 2D barcoding on different size/type of secondary packaging?

8. (If they do not currently produce products with 2D barcoded secondary packaging) What steps (e.g., technology and process) would you need to take in order to produce 2D barcoded secondary packaging on vaccine products?
    a. What would be the cost and lead time associated with implementing 2D barcodes for vaccine secondary packaging per product?
    b. What would be the cost and lead time associated with implementing 2D barcodes for vaccine secondary packaging for all vaccine products?
    c. How much production line down time would be required to transition to 2D barcode labeling on vaccine secondary packaging?

9. If 2D barcodes on secondary packaging for vaccines are adopted as an industry standard, how do you anticipate transitioning fully to 2D barcodes on secondary packaging?

10. How do you currently process secondary packaging information for vaccines?
    a. What vaccine secondary packaging information do you store?
    b. What system(s) do you use to store vaccine secondary packaging information (e.g., inventory management, ERP, logistics)?
    c. What vaccine secondary packaging information do you automatically scan into the system?

11. What data elements would you like to see included in the 2D barcode on vaccine secondary packaging?

12. What steps do you plan to take, specifically related to secondary packaging and inference, to ensure that you are able to maintain e-pedigree information for vaccines (assuming California's Track and Trace legislation is not preempted by the FDA or the Congressional Proposal to Improve Drug Distribution Security)?
    a. How would the FDA or the Congressional Proposal to Improve Drug Distribution Security preempting California's Track and Trace legislation modify your timeline for making technology or process changes to utilize 2D barcodes on vaccine secondary packaging?

13. What do you view as the key drivers and challenges for adoption of 2D barcoding on secondary packaging for vaccines?
    a. Outside of meeting potential future regulatory requirements, what additional benefits do you foresee in using 2D barcoding on secondary packaging for vaccines (e.g., improved accuracy, efficiency, competitive advantage, patient safety, recalls, tracking inventory)?
    b. What, if any, are the most significant challenges you believe would be associated with adding 2D barcoding to secondary packaging for all vaccines?

14. What would be the impact of adopting 2D barcodes for all vaccine secondary packaging on your downstream supply chain partners?
    a. What risk mitigation strategies, if any, could you put in place to mitigate the impact on downstream supply chain partners?

15. Aside from 2D barcodes and barcode scanning, do you know of any other commonly used automated identification technologies for vaccine secondary packaging that exist or are emerging in the market? If so, please explain the benefits/drawbacks of these technologies.

16. Are there any industry trends/forecasts impacting labeling on vaccine secondary packaging that we should be aware of?

Distributors

1. What specific data carriers are used on the secondary packaging of vaccines you receive/distribute (e.g., linear barcode, 2D barcode, RFID, text)?
    a. Where is the data carrier located on the packaging?
    b. Do you add any additional data carriers during the distribution process?
        i. If yes, what type data carrier is added and where is it added to the vaccine packaging?
        ii. Does the data carrier contain product identifying information from the vaccine manufacturer?

2. How do you currently process secondary packaging product information for vaccines?
    a. What information do you store?
    b. What system(s) do you use to store vaccine secondary packaging information (e.g., EHR, immunization registry)?
    c. What information do you automatically scan from vaccine secondary packaging information into the system?

3. How would your technologies or processes need to be altered, if at all, to accommodate 2D barcodes on secondary packaging for all vaccines?
    a. What would be the costs associated with modifying your technologies and processes to utilize 2D barcodes on vaccine secondary packaging?

4. Do you use a data carrier on shipping invoices/manifests for vaccines?
    a. If not, what would be the challenges of incorporating a 2D barcode to your invoice/shipping manifest?

5. What data elements would you like to see included in the 2D barcode on vaccine secondary packaging?

6. What steps do you plan to take, <u>specifically related to secondary packaging and inference</u>, to ensure that you are able to maintain e-pedigree information for vaccines (assuming California's Track and Trace legislation is not preempted by the FDA or the Congressional Proposal to Improve Drug Distribution Security)?
    a. If you plan to use unique barcoding on secondary packaging to support inference, how would you track/maintain line of sight into parent-child relationships for aggregated groups of products?
    b. How would the FDA or the Congressional Proposal to Improve Drug Distribution Security preempting California's Track and Trace legislation modify your timeline for making technology or process changes to utilize 2D barcodes on vaccine secondary packaging?

7. What do you view as the key drivers and challenges for adoption of 2D barcoding on secondary packaging for vaccines?
    a. Outside of meeting potential future regulatory requirements, what additional benefits do you foresee in using 2D barcoding on secondary packaging for vaccines (e.g., improved accuracy, efficiency, competitive advantage, patient safety, recalls)?
    b. What, if any, are the most significant challenges you believe would be associated with adding 2D barcoding to secondary packaging for all vaccines?

8. What would be the impact of adopting 2D barcodes for all vaccine secondary packaging on your upstream and downstream supply chain partners?
    a. What risk mitigation strategies, if any, could you put in place to mitigate the impact on supply chain partners?

9. Aside from 2D barcodes and barcode scanning, do you know of any other commonly used automated identification technologies for vaccine secondary packaging that exist or are emerging in the market? If so, please explain the benefits/drawbacks of these technologies.

10. Are there any industry trends/forecasts impacting labeling on vaccine secondary packaging that we should be aware of?

Providers

1. What specific data carriers are used on the secondary packaging of vaccines you receive (e.g., linear barcode, 2D barcode, RFID, text)?
    a. Where is the data carrier located on the packaging?

2. How do you currently process secondary packaging product information for vaccines?
    a. What information do you store?
    b. What system(s) do you use to store vaccine secondary packaging information (e.g., EHR, immunization registry)?
    c. What information do you automatically scan from vaccine secondary packaging information into the system?

3. How would your technologies or processes need to be altered, if at all, to accommodate 2D barcodes on secondary packaging for all vaccines?
    a. What would be the costs associated with modifying your technologies and processes 2D barcodes to utilize 2D barcodes on vaccine secondary packaging?

4. What data elements would you like to see included in the 2D barcode on vaccine secondary packaging?

5. How would your workflow be impacted if secondary packaging contained 2D barcodes?
    a. Would your workflow be impacted differently for public vs. private purchase vaccines?
    b. Do combination vaccines present opportunities or challenges to leveraging 2D barcodes on secondary packaging?

6. At what point are vaccines removed from their secondary packaging?

7. What steps do you plan to take, <u>specifically related to secondary packaging and inference</u>, to ensure that you are able to maintain e-pedigree information for vaccines (assuming California's Track and Trace legislation is not preempted by the FDA or the Congressional Proposal to Improve Drug Distribution Security)?
    a. How would the FDA or the Congressional Proposal to Improve Drug Distribution Security preempting California's Track and Trace legislation modify your timeline for making technology or process changes to utilize 2D barcodes on vaccine secondary packaging?

8. What do you view as the key drivers and challenges for adoption of 2D barcoding on secondary packaging for vaccines?

9. Outside of meeting potential future regulatory requirements, what additional benefits do you foresee in using 2D barcoding on secondary packaging for vaccines (e.g., improved accuracy, efficiency, competitive advantage, patient safety, recalls)?

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