SERIALIZATION OF PRESCRIPTION DRUGS IN THE USA: A CENTRALIZED VIEW

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ABSTRACT

This thesis explores the impact of the Drug Supply Chain Security Act (DSCSA) on various stakeholders in the pharmaceutical supply chain. Specific attention has been dedicated to the impact on manufacturers and distributors/retailers. Although various interpretations of the DSCSA are possible, this thesis takes the perspective of a centralized data model, and tests the feasibility of implementing a centralized database under both data nesting and unit level relational models. This is in contrast to the decentralized system, which is further explored in the partner thesis, Impact of Drug Supply Chain Security Act on US pharmaceutical industry under decentralized information flow (Chang & Mohan, 2017).

Both quantitative and qualitative analysis are employed in this thesis. Quantitative analysis was conducted using publically available industry data, from which the impact on overall supply chain costs was modeled. Qualitative analysis consisted of stakeholder interviews, process mapping, and time studies to determine the extent of process changes and what they should look like to conform to DSCSA.

After accounting for the current state of implementation, as well as real-world constraints, the findings indicate that the best-practice scenario for Manufacturers and Distributors/Retailers to conform to DSCSA is one using a Centralized data model and nested linked-pedigrees. Although this option is estimated to be 67% costlier than the least expensive scenario, it offers a more robust and secure data model that allows for better long-term scalability. Implementation and cost concerns are also discussed in the conclusion to elaborate on trends and considerations in choosing the appropriate Serialization scenario to pursue.

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Chapter 1: Introduction

1.1 Background

The pharmaceuticals industry has been dogged by counterfeiting and theft since its inception. As an industry, pharmaceuticals make the perfect target: high value products that represent significant returns if falsified and passed off as genuine. This issue has only intensified with increased industry regulation, which raises the cost – and prices – of drugs, making them more attractive to thieves and counterfeiters.

Despite the low incidence of drug counterfeiting and tampering in developed economies, the severity of the consequences is such that it cannot simply be ignored. Take the recent case of counterfeit Avastin found in the US and Canada in 2012. A drug wholesaler acquired counterfeit versions of the popular cancer drug Avastin through an inventory buy-out, and sold the unapproved version to various doctors and medical outlets throughout the US. It should be noted that the wholesaler was not among the approved suppliers of Avastin – however, due to the significant discounts they offered for Avastin, many retail locations decided to purchase from them to reduce costs. Only through intense scrutiny was the counterfeit versions identified as having a different label and incorrect packaging. This event shook public confidence in the pharmaceutical supply chain.

Although the Avastin case was not directly tied to any deaths, the potential for lethal consequences is aptly demonstrated by a similar event. The 1982 Tylenol recall was caused by a case of tampering with over-the-counter (OTC) medicines. Seven people died within several days, each of them having taken tainted Extra-Strength Tylenol. Although Johnson & Johnson was able to recover their reputation and the brand by taking decisive action, the costs ran into the hundreds of millions of dollars. Tampering with OTC medicines and replacing the contents with poison is a different crime than counterfeiting; however, the risks to both the consumer and the companies involved are very comparable. It does not require a stretch of the imagination to see that counterfeit drugs could cause unintended lethal consequences, and it is in the best interests of the entire pharmaceutical industry to
ensure this is closely monitored and prevented. As tragic as the Tylenol is, it should be noted that cases like these occur much more frequently in developing and under-developed countries.

In order to deal with these dangers, drug traceability measures have been passed in many countries to increase supply chain visibility. By taking steps such as unique serialization of all drugs produced, regulatory authorities will now have the ability to trace their product through the supply chain to determine where it came from, and where it was distributed to. Furthermore, the serial number could serve as an obstacle to theft or counterfeiting of drugs. Not only would potential criminals need to replicate the entire packaging and appearance of the drug, but they would also need to either provide a correct serial number that matches up against the database of valid drugs, or to manipulate the table to match their fake serial number.

Although primarily a regulatory requirement (for ease of carrying out recalls, or identifying specific loss points in the supply chain), implementation of serialization may promise potential benefits to both companies and consumers. Turkey, India, China, and Brazil have been among the first countries to implement pharmaceutical serialization legislation, with varying degrees of success (Davison, 2011). System architecture differs one from another, for example Turkey uses GTIN, Serial number, Lot and Expiration (Dates that are market on the product); while Europe is using the EFPIA concept – the harmonization of pharmaceutical products codification throughout Europe.

In all of these cases, the driving force behind serialization was the ability to verify products through the entire supply chain, with the added potential for track & trace. With increases in technology capability of storing large amounts of data, as well as improved serialization capabilities, many national governments have seen fit to introduce similar legislation to take advantage of new technological capabilities.

The United States is no exception to the rule. In late 2013, Congress passed the Drug Supply Chain Security Act (DSCSA), which stipulated the measures that manufacturers, distributors, and retailers needed to take, starting in 2015 and to be completed in 2023, of adhering to tracking and
tracing requirements. The law mandated that all manufacturers had to put in place product tracing requirements at a lot or batch level by 2015, and serialized product identifiers by start of year 2017. Furthermore, full item-level traceability for all products, from manufacturers through to end retailer, should be achieved by 2023. (U.S. Food and Drug Administration, 2014).

Although the DSCSA was inspired by the laws implemented overseas, it differs from foreign legislation in a few key areas. As opposed to China, which had a government-mandated, centrally organized database for all serialized drug products, the US has not prescribed a serial-number storage system. Similarly, although the EU has undertaken serialization efforts as well, they are faced with differences in national interpretation, a problem that the US does not face.

Because of the relative degree of freedom afforded by the DSCSA, a couple key questions remain to be answered: What type of data storage system should be utilized for serialization in the US, a centralized system managed by one player, or a decentralized system that is maintained ad-hoc by everyone involved? How should manufacturers and distributors pack and record their shipments? With individual SKU level traceability expected in the long-run, how can companies keep the data-nesting requirements presented by current packaging standards (pallet=>case=>box=>SKU) manageable?

1.2 Purpose

As discussed briefly in the previous section, the DSCSA presents a number of challenges that are not clearly outlined, or have been left to pharmaceutical industry players to decide on and clarify. Chiefly among these, is the method by which serial numbers should be stored, shared, and transmitted. This we will term the data model for serialization. Secondarily, a challenge exists around defining an appropriate standard for linked pedigrees – the way that each individual unit is tied to its parent carton, case, or pallet – and this we will term the Relational model for serialization.
Our thesis offers an objective, third party view of the DSCSA, and provide recommendations, based on both current practice, as well as theoretical capability, that will help align industry players with the law. As part of the analysis, this thesis will include both qualitative as well as quantitative analysis to support our recommendations. The pertinent measurements are chosen based on interviews with current industry stakeholders. Quantitative analysis is conducted using publically available industry data, from which the impact on supply chain costs, lead times, and capital investments could be estimated. Qualitative analysis consisted of stakeholder interviews, process mapping, and time/motion studies to determine the extent of process changes and what they should look like to conform to DSCSA.

1.3 Terminology

Below is a list of abbreviations and terms used in the process models:

- **EPCIS** – Electronic Product Code Information Services, the global GS1 standard for creating and sharing visibility event data
- **EDI** – Electronic Data Interchange, the exchange of data between companies/organizations
- **TH** – Transaction History
- **TS** – Transaction Statement
- **TI** – Transaction Information
- **Manufacturer (MF)** – The manufacturer of the actual pharmaceutical drug; in control of the active pharmaceutical ingredient (API)
- **Wholesaler (WS)** – The wholesale distributor of the pharmaceutical products; these can take the form of large bulk-buy players who play the middlemen in the supply chain, or repackagers who purchase the pharmaceuticals in bulk and repackage them for resale in smaller quantities
• Self-Distributing Dispenser (SDD) – Self-Distributing Dispensers encompass those firms that buy directly from the pharmaceutical manufacturer, and sell directly to the end consumer. These firms usually possess their own warehousing and repackaging capabilities, as well as their own retail outlets. Examples of Self-Distributing Dispensers include retailers such as Walgreens, CVS, Rite Aid, and Wal-mart

• Dispensers (DS) – Dispensers include smaller retail outlets that purchase pharmaceuticals from wholesalers and repackagers, and handle sales of pharmaceuticals to consumers. Dispensers are usually smaller operations without significant warehousing or repackaging capabilities. Examples include independent drugstores and most hospitals.

• Linked pedigrees – a data structure that traces each individual consumer unit through its life cycle, so that one may see the origin, or “pedigree” of the product. Linked pedigrees make tracking drugs through their many package iterations possible. Sometimes also referred to as the “inference model” of data nesting.

• Matroyshka format – similar to the concept of linked pedigree. However, Matroyshka format explicitly refers to a parent-child linked pedigree relationship where each parent will have many children. (ex: one pallet may contain 56 cases, and each case may contain 80 units). Also referred to as Russian Doll format.

Chapter 2: Literature Review

In recent years, as the pharmaceuticals market has grown, so has its attractiveness to criminals and dishonest businesses. Drug theft has always been a problem, and the lucrative industry has seen its fair share of legitimate drugs turn up on the international black market. Furthermore, counterfeit drugs have become increasingly prevalent in recent years, buoyed by growth in both the open market as well as the black market. With this trend comes the potential for serious consumer
harm from ingesting adulterated versions that have no effect on the illness they are prescribed for. On the contrary, counterfeit and adulterated drugs themselves may cause more harm than good.

Pharmaceutical serialization is one method proposed to counter drug counterfeiting and theft. Although not an entirely sufficient solution within itself, it closes many of the loopholes currently in existence. By assigning serial numbers to each discrete drug unit, both drug manufacturers and distributors will be better equipped to track and trace their drugs throughout the entire supply chain. This will make theft easier to detect and identify, as well as make the introduction of counterfeit drugs more difficult. Towards this end, the FDA has mandated the implementation of drug serialization efforts in the form of the Drug Supply Chain Security Act (DSCSA) by 2017 for manufacturers, 2018 for distributors, and 2019 for contract manufacturers.

However, as simple as serialization may seem, it contains significant data generation, transmission, and verification challenges. Not only will serial numbers need to be generated for each drug unit, but that data must be stored and made available for validation by any player within the supply chain. The technological challenges of running an effective serialization effort also extend to the physical supply chain. Serial numbers will need to be physically printed or tagged on each drug unit, and consolidation of units for shipment will need to be subject to the system ability to create “nested” linked pedigrees that contain all serial numbers tied to the shipment.

This literature review answers a couple key questions behind the composition and implementation of a successful serialization effort.

1. What is absolutely necessary for a successful serialization effort, from both a legal and practical point of view?

2. How have other regions carried out serialization, and what has/has not worked in those cases?

3. What are the best practices that should be carried forward in any US-based serialization effort?
2.1 Previous Research

Serialization has been a hot topic in pharmaceutical circles in the last three years due to the passage of the Drug Supply Chain Security Act, and a large quantity of literature has begun accumulating on the subject. A certain level of agreement has been reached regarding the keystones that frame the DSCSA, among them, Serialization, Track & Trace, and Verification (La-Torre Snyder, 2016).

1. Serialization

Serialization is the process that underpins the entire logic of the DSCSA. As defined by Laskowski and Imeraj, 2016, serialization is the “unique assignment of a serial number in conjunction with individual production data as data matrix code (product identification GTIN/NTIN/PPN, expiration date, and batch number)”. This process ensures the product against unwanted tampering, and guarantees its authenticity (insofar as the packaging integrity can be maintained).

Although serialization is a straightforward process, the product and packaging can pose challenges. Labels on circular bottles, for example, pose positioning challenges for documentation scanners when bottles are moving along a production line (Shanley, 2016). Furthermore, learning from companies that have already taken steps to implement serialization has revealed that product aggregation capabilities must be developed alongside serialization capabilities. Not doing so risks not taking aggregation requirements into consideration when implementing the serialization technology, leading to rework and a delayed implementation (Shanley, 2016).

Further discussion of serialization centers on its importance in any track and trace initiative, and the fact that companies should actively invest in this technology, instead of adapting a “wait and see” strategy and taking the easiest or most direct solution. This is illustrated by Lori Clapper
in her article on China’s serialization efforts. One of the major issues encountered in this government-led initiative was the implementation of a standardized product identification code that may prove incompatible with global formats. By taking the most direct step of issuing national product identifiers, China may have set back its own efforts by erecting an additional barrier to data interchangeability with global product identification standards (Clapper, 2013).

2. **Track & Trace**

Track and trace describes the ability of the supply chain to determine where pharmaceutical goods will be. If tracking were thought of as the forward-view, then tracing would be the historical view (LaTorre-Snyder, 2016). The challenge of traceability lies in the need to comply with international counterfeiting requirements, management of multiples of serial numbers under aggregation conditions, as well as reconciliation of used and discarded serialization numbers (Laskowski & Imeraj, 2016).

3. **Verification**

The last building block of serialization consists of verification. This step encompasses the end node of the supply chain, whether that be the retailer or the end customer, being able to verify the contents and identity of their drug unit against a data repository. At the same time, the requirement also holds for points in the reverse supply chain; product returns to the wholesaler or manufacturer would also need to be verified. Any effort at implementing a successful verification system needs to revolve around Electronic Product Code Information Services (or EPCIS). While the technology for EPCIS is being continuously developed for use with serialization, there has yet to be a viable alternative (Shanley, 2016).

While many articles explore the legal and theoretical framework of serialization, more recent papers have looked into the practicality of implementation. In *Serialization in the Pharmaceutical Industry* (Cordon et al., 2016), the authors propose that the implementation of serialization could have many flow-on benefits for companies. These include the potential for expanding business model
to include health data management, improvements to the value chain, as well as better customer data. Furthermore, Cordon posited that the impact of track and trace implementation on actual manufacturing output would be minimal in the first phase of serialization, which only requires labeling of each individual consumer unit. However, as companies begin to expand serialized product across their supply chains, bottlenecks may appear and start to impact efficiency of operations.

Although pharmaceutical is one of the first industries with a regulated effort to implement serialization, it is not the only industry that has tried. Parallel efforts have been undertaken with tobacco and alcohol products, as it has been with certain foods and beverages (Davidson, 2011). In those markets, the regulation aspect is optimized around taxation, giving a very different impetus than that of pharmaceutical regulations. However, the lessons learned from implementation of tobacco and alcohol tracking in countries like Turkey can still prove valuable in understanding the effectiveness of track & trace methods. Options used include the hardware and software tracking of individual units, as well as security inks needed to aid product identification.

Perhaps the most thorough review of pharmaceutical tracking is given in the book *Pharmaceutical Anti-Counterfeiting: Combating the Real Danger from Fake Drugs* (Davison, 2011). In addition to discussing the rationale behind the global movement towards serialization, a number of pertinent technologies are discussed. These include current barcode technology, 2D datamatrix barcode technology, RFID, and packaging fingerprinting. The advantages and limitations of each are discussed; for example, although linear and matrix barcode technology is developed and reliable, implementation would require a line-of-sight to be established from the reader to every single item in a pallet – a daunting task. On the other hand, RFID allows reading radius to be adjusted, and does not rely on line-of-sight to gather information. Unfortunately, the best RFID technologies still only have an accuracy rate of 99%, which is an unacceptably low accuracy rate for this industry.

Two methods of implementing track and trace were proposed in by Davison; the inference approach, which uses linked pedigrees to identify products as they moved through the supply chain,
and the bookend approach, which uses two set reference points in the supply chain to validate receipt and distribution of pharmaceutical products. Both offer unique advantages and disadvantages. The inference approach requires each player in the supply chain to be equipped to aggregate and disaggregate multiple pack levels, while also having the ability to pass multi-level pedigree information securely from one player to the next. This ensures full visibility throughout the supply chain, and offers the best deterrent to counterfeiting, as drugs are securely monitored and documented at each step.

On the other hand, the bookend approach is much easier to implement, requiring only two checkpoints (at the manufacturer and at the dispenser). The drugs produced would be labeled individually, with pick and pack occurring normally. The drugs would not be tracked through the supply chain; as intermediate players would not be required to ascertain the validity of their product. However, once at the dispenser, each unit is individually verified against a central manufacturer database to ascertain authenticity. Although this approach offers decent traceability at a fraction of the effort to implement a full Inference approach, it does have flaws. One such flaw is the theoretical ability for counterfeiters to insert fake goods mid-stream. As long as the counterfeit goods are the first ones to reach the dispenser, and assuming they have a correct serial number, they would be accepted as genuine product.

Another key consideration of serialization lies in the technology used to ensure track & trace security. A deep dive of existing EPCIS technology is presented in the paper, "EPCIS Event-Based Traceability in Pharmaceutical Supply Chains via Automated Generation of Linked Pedigrees" (Brewster & Solanki, 2014). In their investigation of Pharmaceutical traceability technology, they’ve identified the need to separate data generation into three events: ObjectEvent, AggregationEvent, and TransactionEvent. These events correspond to points in the process where individual pharmaceuticals are serialized, packed, and shipped/received. Using the existing EPCIS (Electronic Product Code Information Services) standards for pedigree generation, Brewster and Solanki attempted to model
the type of setting and systems needed to carry out serialization across a high volume supply chain. In their estimates, although varying the item/case and case/pallet count had little impact on the time for pedigree generation, the time needed for checking these pedigrees increased exponentially. When considering the importance of counterfeit detection in a track & trace system, one can see that existing EPCIS standards are not without their downsides.

While pharmaceutical serialization efforts have only just gotten started in the US, there is already a fair amount of learning from which we can draw on to establish best practices going forward. Various early adapters have discovered the implementation methods that work, alongside those that do not, and parallel efforts abroad have showed us that a working solution does not always have to align with the original legal intent (Clapper, 2013). Based on existing literature, it would seem fair to say that any future serialization efforts should place sustainability of the operation (ease of aggregating and disaggregating data, use of international coding standards, choice of data management systems that can integrate with manufacturing execution systems) at the forefront to ensure long term viability.

Perhaps the best lesson to be taken, however, is that serialization poses both a great challenge and a great opportunity. With both physical and information components in play, companies that make a heavy investment into a robust, scalable serialization system stand to gain both financially as well as legally (Daleiden). The bottom line remains; in order for pharmaceutical players to remain relevant in the fast-changing legal landscape, they must adapt to the new requirements, and adapt well, to thrive.

Chapter 3: Process Models

3.1 Current Process

In order to assess the impact of serialization on today’s pharmaceutical supply chains, we first analyzed the current process to understand the data touchpoints. The pertinent players in this
process model include the Manufacturer (maker of the drug), the Wholesaler (bulk purchaser and distributor of the drug), the Self-Distributing Dispenser (large integrated wholesaler-retailers of drugs), and smaller Dispensers (mom-and-pop pharmacies). In many cases, the supply chain would only consist of three players (MF, WS, DS, or MF, WS, SDD). However, to maintain consistency, all four players have been modeled as seen in Figure 1.

The current information tracking process does not contain any serialization steps beyond basic lot identification undertaken at the point of manufacture. Factory markings are applied to each unit of product as they leave the production line indicating the lot batch. This information is also printed on packaging cases. On outbound, this information is kept to identify which customer has received which lot(s) of drugs.

Data Exchange Model - Centralized

![Data Exchange Model](image)

When the need to cross reference drug lots arises, the manufacturer can take the lot code from the drug unit in question and cross reference it against the internal manufacturing database. In
essence, this is already a centralized database operation where any product issues are redirected and referenced against the manufacturer database.

3.2 Future Process: Centralized database, Matroyshka relational model

To adequately implement serialization going forward, a number of steps need to be taken to make data handling practical. The most important of these steps will take place at the outbound shipment point from the manufacturer. Once the customer order is received, the manufacturer will need to identify the specific cases/pallets that are being shipped to the customer, and map that data to the serial numbers of each product unit included in the shipment. This data will then be aggregated, associated with the shipment number, and sent downstream via EDI (Figure B).

Outbound Shipment Process (Russian Doll)

Figure 2 - Outbound Shipment Process Matryoshka

On the wholesaler inbound side, the shipment will be received, and the cases/pallet number scanned, to ascertain that correct product has been received. In a centralized model, the case and pallet numbers should directly reference the aggregated serial number data from the manufacturer, negating the need for the wholesaler to individually scan and receive each product unit. However, in
certain cases where the pallet and case numbers may be missing or unreadable, the individual serial numbers of each product unit will need to be received in individually.

If the received product serial numbers do not match the information provided by the manufacturer, the wholesaler will need to follow the normal exceptions process and put the product on quarantine. This product will remain in quarantine status until the data has been verified from the Manufacturer regarding their authenticity. Upon successful verification, the serial data will be copied to the Wholesaler database and marked as received (Figure 3).

**Inbound Receipt Process (Russian Doll)**

![Inbound Process Matryoshka Diagram]

*Figure 3 - Inbound Process Matryoshka*

When it comes time for the wholesaler to distribute individual units/cases to the retailer level, the serialized product will follow a similar process to the manufacturer outbound process; each product unit will be scanned and verified against existing inventory, and the information aggregated to the shipment number. Upon completion of pick and pack operations, the serial data will be transferred downstream via EDI, at the point of change of financial ownership.
3.3 Future Process: Centralized database, Unit Level relational model

Although it seems logical that a Matroyshka relational model that uses nested data clusters to trace product pedigree would be preferred in a centralized database, possessing this level of functionality poses an additional level of difficulty that could be bypassed if the relational model was only implemented at a unit level. To these ends, a future process map using a Unit Level relational model was created to visualize the process.

In Figure 4, we see that a Unit Level outbound shipment process bears many similarities to the Matroyshka model; however, the aggregation responsibility of individual product units now falls on the downstream partner (wholesaler, distributor). The potential time expense needed to receive and consolidate the individual serial number information could prove to be quite time consuming.

Outbound Shipment Process (Unit Level)

Figure 4 - Outbound Shipment Process Unit-level

On the inbound side, each individual unit will be scanned and verified against the centralized database at the manufacturer to ascertain authenticity of product. If the product received does not match the serial data contained at the manufacturer level, the product will need to be put on hold until
authenticity can be verified. Although tedious and time consuming, this process offers the potential of being much more accurate than having a Matroyshka relational model: as each individual serial number is scanned in and out at each hand-off point in the supply chain, they are individually validated, instead of validated en masse. This process is shown in Figure 5.

**Inbound Receipt Process (Unit Level)**

![Diagram of the Inbound Receipt Process (Unit Level)](image)

*Figure 5 - Inbound Process Unit-level*

The last step here is identical to what it would be under a Matroyshka relational model – since retail sales are conducted in consumer units, each individual unit would be scanned to mark that it has been sold. This process would not differ under either scenario.

### 3.4 Assumptions

In our process models, we have made a number of assumptions around operating conditions and processes:
- It is assumed that the process of transferring ownership from Manufacturer to Wholesaler is identical to the process of transferring ownership from Manufacturer to Self-Distributing Dispenser, and that the physical process will remain the same (e.g. Bills of lading will not contain unit level serial numbers, but pallet numbers). Track and Trace will be predicated similarly on the transfer of financial ownership.

- It is assumed that the Self-Distributing Dispenser will not need to validate each product serial number shipped to its own retail outlets; however, the product will need to be scanned and taken out of the system upon sale.

- It is assumed that third-party logistics companies will play no part in the interchange of serial data and verification of serialized product.

Chapter 4: Methodology

4.1 Research Methodology

The research methodology for this thesis consisted of both primary and secondary research. Due to the unique circumstances of this thesis (i.e., written as an evaluation of the impact of DSCSA), it was felt that secondary research alone (review of both academic literature as well as recent news and industry publications) would not capture all considerations on this topic. For this reason, primary research was undertaken by interviewing current employees of both a large pharmaceutical manufacturer and a large self-distributing dispenser. These interviews were targeted at understanding the primary risks, costs, and considerations of current players in the industry.

Interviews were conducted both in person, as well as over the phone, during the period of Fall 2016 through Spring 2017. Primary interviews were drawn from two large players in the pharmaceutical industry; One is a multinational manufacturer of prescription and over the counter drugs, while the other is a large wholesaler/dispenser of drugs in the North American market. The
interviews drawn from these two companies were assumed to be in alignment with other industry players.

4.2 Analysis Methodology

The analysis of the impact of DSCSA, and serialization in particular, on the pharmaceuticals supply chain was carried out by modelling the financial and inventory impacts in a hypothetical network. Information gathered during the interview process indicated that, in order to measure the relative costs and advantages of each possible serialization model, estimates for each individual cost factor needed to be drawn up. These cost factors were determined to be: Ongoing Operational Costs, IT Investment Costs, and Capital Expenditures (hereafter referred to as Capex). Each of these cost factors were individually estimated using a bottoms-up methodology, using industry data available through public sources, and validated for directional accuracy with the thesis sponsor team to ensure applicability to the industry. The costs listed in this section should be considered on a relative scale instead of an absolute scale for that reason.

Eight distinct scenarios were determined based on a combination of the data model and the relational model. Within the data model, four possible options were available: Centralized – Manufacturer lead, Centralized – 3rd Party lead, Centralized – Government lead, and Decentralized. Within the relational model, two options existed: either Unit Level tracing, or Matroyshka format linked pedigree tracing. A combination of these two model options result in the eight distinct scenarios mentioned. The full tables for each scenario is provided in Figure 6.
4.3 Cost Categories

Ongoing Operational Costs

The first cost category, Ongoing Operational Costs, was built based on the assumption that Serialization using the Matryoshka relational model would require additional labor and equipment maintenance to implement effectively. This approach modeled the time necessary to complete each step of the packing, shipping and receiving process, and then estimates the total costs. Information was collected on the number of individual cases required, and the number of cases per pallet, as well as the steps required at each stage in the process. Average time per task was obtained through interviews with industry stakeholders. An industry average labor cost rate was then used to convert the total operational time required to a cost figure. The formula and Figure 7 below illustrate the Operational Cost calculation method:

\[
\text{Operational Costs} = \text{Minutes per task} \times \text{Annual Volume} \times \text{Hourly labor rate}
\]
Outbound shipment process

<table>
<thead>
<tr>
<th>Process steps</th>
<th>Time Req'd (Minutes)</th>
<th>Unit</th>
<th>Volume</th>
<th>Total Time (Minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Picking full pallets and scanning at unit level</td>
<td>86.4</td>
<td>Minutes/Pallet</td>
<td>762,220</td>
<td>65,855,836</td>
</tr>
<tr>
<td>Case picking and scanning at unit level</td>
<td>1.44</td>
<td>Minutes/Case</td>
<td>10,671,085</td>
<td>15,366,362</td>
</tr>
<tr>
<td>Each/Unit picking and scanning at unit level</td>
<td>0.06</td>
<td>Minutes/Unit</td>
<td>91,466,439</td>
<td>5,487,986</td>
</tr>
<tr>
<td>Consolidating shipment</td>
<td>5</td>
<td>Minutes/Shipment</td>
<td>42,346</td>
<td>211,728</td>
</tr>
<tr>
<td>Loading and shipping</td>
<td>0.488</td>
<td>Minutes/Shipment</td>
<td>42,346</td>
<td>20,665</td>
</tr>
<tr>
<td><strong>Total Cost</strong></td>
<td><strong>$ 24,198,293</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 7 - Operational Costs

**IT Investment Costs**

The second cost category, IT Investment Cost, is calculated using a combination of the investment necessary in storage space, as well as the cost of setting up the data interfaces between partners in the supply chain. Storage space investments include the capital expenditures on physical assets (servers and racks), as well as the cost of cloud storage if managed by a 3rd party. The cost of setting up data interfaces includes all the IT implementation costs associated with integrating the serialization database with the existing IT architecture at all levels of the supply chain and testing it for robustness. This portion includes both a one-time cost, as well as an ongoing annual cost.

The IT costs have been calculated based on the number of storage requirements and transactions required per each echelon. It also considers that at each point of transaction all the information will be provided by the receiver of the product. The input data required is provided in Appendix 4.

From the primary research with one of the 3rd party service providers we could see the following costs considerations:

- Annual Subscription Fee
- One-time implementation cost
- Set up connections with each supplier where each connection is charged on individual basis.

The rough cut estimation show that the 3rd Party company would provide the cheapest services based on the quote. However, there is a risk for the industry players to fully rely on an
individual 3rd party system provider in the long run. The initial cost attractiveness could make the industry dependent on one company. If monopoly status is achieved the 3rd Party service provider could possibly increase the subscription fee, which will undermine the attractiveness of such solution.

While the Ongoing Operational Costs are largely the same regardless of the data model or the relational model, IT Investment Costs differ greatly among the various scenarios. Depending on the data model, the IT Investment Costs could be borne by the manufacturer and the pharmaceutical supply chain, or by an outside player to the pharmaceutical industry such as a 3rd party service or the government. In either of these latter cases, the overall IT capital expenditure for pharmaceutical players would be greatly reduced; however, the variable cost of yearly operating fees would increase. Figure 8 below shows the IT Investment Cost calculation method, alongside an example.

Example:

\[
IT \text{ Investment One-time Cost} = \left(\frac{\text{Annual Production Volume} \times \text{Data Storage needed}}{\text{Storage Capacity per server}}\right) + \left[\text{Number of downstream supply chain partners} \times \text{Cost per database linkage}\right]
\]

\[
IT \text{ Investment Recurring Cost} = (\text{Annual maintenance hours needed} \times \text{Labor cost per hour})
\]

<table>
<thead>
<tr>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>annual production QTY</td>
</tr>
<tr>
<td>required storage year</td>
</tr>
<tr>
<td>unit data volume for TS/TH/TI (Byte)</td>
</tr>
<tr>
<td>Annual Data Volume (GB)</td>
</tr>
<tr>
<td>Cloud Data Storage Cost/GB/Year</td>
</tr>
<tr>
<td>Data Storage Cost</td>
</tr>
</tbody>
</table>

Figure 8 - IT investment Manufacturer example
One Time Capex Costs

The third category, Capital Expenditures, also differs significantly depending on the individual scenarios. In this case, the cost difference is driven by the distinction between a Matroyshka relational model vs a Unit Level relational model. In a Matroyshka model, the capital expenditures are expected to be higher due to the added granularity of data aggregation. In a Unit Level model, some of the equipment would not be necessary. In each case, production volume was used to determine the quantity of equipment needed to obtain sufficient serialization capacity, and financial data around machine costs were used to determine the total investment cost.

In order to understand what are all the on-time costs this research considers several costs and sub-cost variables. It considers all the echelon types such Manufacturing facility, Manufacturer Distribution Center, Pharmacy, Wholesaler and Repackager. Each individual echelon incurs its own costs, which are mainly related to the processes that will change as the result of serialization. The Manufacturing facility will acquire costs on change in its outbound process as well as it will have to make capital investment into serialization of the material. The Manufacturer Distributions Center (Manufacturer DC) would also acquire the same costs in case of Matryoshka model where de-casing, repackaging and serialization of the new boxes will be required. In addition, the Manufacturer DC will have the change of the inbound process, which requires the de-casing assets to be installed. The Wholesaler is considered to have similar investment scheme for the inbound process as Manufacturer DC, whereas the outbound process will be different. Based on the primary research with the industry representatives the Wholesaler ships circa 97% of the product to the pharmacies on the unit-level basis. Therefore, for this research we consider that the wholesaler will not have the aggregation process at the outbound logistics.

The unit-level or Matryoshka level defines the capital intensity and the volume of production that will go through the whole supply chain.
Figure 9 below shows the different cost variables that are associated with the serialization at the Manufacturer facility:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Costs Associated with the Variable</th>
<th>Subcost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Matryoshka Line upgrade for serialization</td>
<td>Factory size increase and preparation</td>
<td></td>
</tr>
<tr>
<td>Matryoshka Line upgrade for serialization</td>
<td>Label redesign and FDA Supplemental New Drug Application (sNDA) approval</td>
<td></td>
</tr>
<tr>
<td>Matryoshka Aggregation equipment in warehouse</td>
<td>Optel Warehouse Station includes everything you need to print, apply, capture, verify, rework, decommission, submit serial numbers and ship in your warehouse.</td>
<td></td>
</tr>
<tr>
<td>Matryoshka Line upgrade for serialization</td>
<td>Integrated unit level serialization equipment (Print, Pack, Apply)</td>
<td></td>
</tr>
<tr>
<td>Matryoshka Aggregation equipment in warehouse</td>
<td>Installation costs</td>
<td></td>
</tr>
<tr>
<td>Matryoshka Line upgrade for serialization</td>
<td>Safety stock (Inventory holding) for installation time</td>
<td></td>
</tr>
<tr>
<td>Matryoshka Aggregation implementation costs</td>
<td>Training</td>
<td></td>
</tr>
<tr>
<td>Matryoshka Aggregation implementation costs</td>
<td>Project Management</td>
<td></td>
</tr>
<tr>
<td>Matryoshka Line upgrade for serialization</td>
<td>Vision Equipment</td>
<td></td>
</tr>
<tr>
<td>Matryoshka Line upgrade for serialization</td>
<td>System integration of software and hardware</td>
<td></td>
</tr>
<tr>
<td>Matryoshka Line upgrade for serialization</td>
<td>Installation costs</td>
<td></td>
</tr>
<tr>
<td>Matryoshka Line upgrade for serialization</td>
<td>Installation costs</td>
<td></td>
</tr>
<tr>
<td>Matryoshka Line upgrade for serialization</td>
<td>System integration of vision software and hardware</td>
<td></td>
</tr>
<tr>
<td>Matryoshka Line upgrade for serialization</td>
<td>Training</td>
<td></td>
</tr>
<tr>
<td>Matryoshka Line upgrade for serialization</td>
<td>Checkweighing equipment/Scanner/Camera</td>
<td></td>
</tr>
<tr>
<td>Unit-level Aggregation equipment in warehouse</td>
<td>Warehouse storage increase due to increased inventory</td>
<td></td>
</tr>
<tr>
<td>Unit-level Line upgrade for serialization</td>
<td>Factory size increase</td>
<td></td>
</tr>
<tr>
<td>Unit-level Line upgrade for serialization</td>
<td>Label redesign and FDA Supplemental New Drug Application (sNDA) approval</td>
<td></td>
</tr>
<tr>
<td>Unit-level Line upgrade for serialization</td>
<td>Integrated unit level serialization equipment (Print, Pack, Apply)</td>
<td></td>
</tr>
<tr>
<td>Unit-level Line upgrade for serialization</td>
<td>Vision Equipment</td>
<td></td>
</tr>
<tr>
<td>Unit-level Line upgrade for serialization</td>
<td>System integration of software and hardware</td>
<td></td>
</tr>
<tr>
<td>Unit-level Line upgrade for serialization</td>
<td>System integration of vision software and hardware</td>
<td></td>
</tr>
<tr>
<td>Unit-level Line upgrade for serialization</td>
<td>Training</td>
<td></td>
</tr>
<tr>
<td>Unit-level Line upgrade for serialization</td>
<td>Safety stock (Inventory holding) for installation time</td>
<td></td>
</tr>
<tr>
<td>Unit-level Line upgrade for serialization</td>
<td>Checkweighing equipment/Scanner/Camera</td>
<td></td>
</tr>
</tbody>
</table>

Figure 9 - Manufacturer Capex on Serialization
In order to calculate approximate number of each individual equipment required, the throughput of the material per machine and the total number of individual units produced per year is considered.

**Example:**

\[
\text{Investment in integrated unit level serialization equipment} = \text{Number of equipment required} \times \text{Cost of individual equipment}
\]

\[
\text{Number of equipment required} = \frac{\text{Total Yearly Production}}{(\text{Throughput of a Machine Per Minute} \times 60 \text{ minutes} \times 8 \text{ hours/day} \times 20 \text{ days/month} \times 12 \text{ months/year})}
\]

Cost of individual equipment is calculated with the assumption that the industry will use the 2D barcode. For this research, we performed the secondary and primary research with the equipment providers. Costs of the machines were quoted by equipment producers, however, should only be taken as a guidance for university research. The real price quotes should be negotiated with the suppliers on individual basis.

One of the outcomes of the research on the Capex costs for Manufacturer Facility is that the majority of the costs will be incurred due to

- Warehouse storage increase due to the increased inventory holding
- Factory increase due to serialization equipment installation
- Label redesign and FDA Supplemental New Drug Application (sNDA) approval – calculated based on the costs per individual engineer
- Integrated unit level serialization equipment
These four factors account for most of the cost for manufacturer.

Safety Stock

The equipment providers suggest manufacturer to consider the safety stock holding to cover for the equipment installation time. The downtime of the production due to the equipment installation is very difficult to predict. It will also depend whether the manufacturer operates on the full capacity and cannot perform installation during the low load time. Considering the half day installation time for all the equipment the industry needs to build a substantive safety stock. The safety stock will not be the factor of the Capex, however, will affect the working capital for the companies for the year of the installation.

The estimated safety stock for the whole industry is calculated through the inventory benchmark. It considers the units that are not produced during the installation time multiplied by the cost of the product.

These costs cover most of the total costs, however, it does not consider all the industry costs. Some of the additional implementation costs should be considered by the industry (Appendix 2). Appendix 3 gives a detailed breakdown of estimated costs for each individual echelon. The figures combine the safety stock costs; however, it also provides the figure without safety stock.

Total costs were then obtained by summing up the Operational, IT, and Capex necessary for each scenario.

Chapter 5: Discussion of Results & Implications

5.1 Results

Using the above mentioned methodology, the total costs for each of the eight distinct scenarios was determined for a 10-year timeframe. In order to accurately compare the costs between the Centralized and Decentralized data models, all costs were measured in proportion to the least
The findings from our analysis suggest that serialization using a Centralized data model would in all cases incur a higher proportional cost than using a Decentralized model. The cost premium to using a Centralized data model range from 67-96%; a massive cost premium. The financing of such a Centralized database could also pose a problem due to the high level of investment required. Although a Centralized data model would offer much more efficient operations and better track and trace capability, the expenses of investing in and maintaining a sufficient data storage and management capacity far outweigh the efficiency cost savings of being able to reference a single source of truth.
However, before a final evaluation can be made regarding the suitability of Centralization or Decentralization of the data model, qualitative considerations regarding data integrity and database resilience must be taken into account. Decentralization of the database poses a risk of creating duplicate data versions, and also presents the challenge of ensuring data is passed efficiently between supply chain partners. For this reason, although a Decentralized data model is the financially logical decision, it may be qualitatively unfeasible and present issues of scalability for smaller organizations.

Furthermore, data security and access poses a major cause for concern for both cases; who should have the ability to access and manage a database, whether Centralized or Decentralized? It goes to reason that a Centralized database should have much closer security controls to manage access, but the concern is equally valid for a Decentralized model, where access to different parts of the data may be spread among many users. In the Figure 11 - Comparison of System Architecture Types we provide an extensive, although not exhaustive, list of different considerations that should be taken by the industry.
On the other hand, a Centralized data model is not without its own challenges. The capability needed to host a centralized database, which can also handle repeated verification checks from across the supply chain, could put immense strain on existing information networks. Investment in resilient database systems to ensure reliability is recommended. At the same time, security and integrity must be top concerns. A security breach in a centralized database would be infinitely more dire than in a decentralized system.

Financially, a Centralized model could prove to be relatively less expensive than estimated under certain conditions. If labor costs rise prodigiously, then the additional manual querying required in a Decentralized data model could incur larger costs than currently estimated. Along the
same lines, if data storage costs dropped significantly, then Centralization of the data model would result in the most efficient form of data storage, giving the lowest storage costs for the long term.

Pharmaceutical inventories would see the highest temporary increase in a Matroyshka relational model due to the longer line shutdown time required to install serialization equipment. However, a Matroyshka relational model would have a negligible effect on long term inventory or cycle time – once the equipment is installed, the physical process essentially reverts back to normal.

On the other hand, a Unit Level relational model would increase the cycle time and create a permanent, albeit slight, increase in inventory. Longer lead times generated from more time-consuming processes on both outbound and inbound receipts are the primary responsible factors behind this permanent inventory increase. It can also be assumed that an increase in inventory would have flow on effects of increasing the amount of storage space required, which may result in heavier capital expenditure investments in warehousing capabilities.

It is also possible to combine aspects of the different centralized and decentralized scenarios through the whole supply chain. The most likely scenario is going be a hybrid of the Centralized and Decentralized scenario with Matryoshka aggregation at the downstream of the supply chain. shows the different scenarios of the supply chain dynamics. The Figure 13b - Most Likely Scenarios depicts the scenarios that are most likely to happen.
97% of the product sent on the unit level

**Figure 12a - Most Likely Scenarios**
97% of the product sent on the unit level

**Distribution:**
- Specialty Distributor: 10%
- Independent Dispenser/Pharmacy: 10%

**Volume:**
- Inbound Unit-level: 70%
- Outbound Unit-level: 30%

**Matryoshka 3rd Party Company:**
- Wholesaler (Distributor): 12%
- Manufacturer Facility: 8%
- Unit-level Direct Shipments: 10%

**Other:**
- Other: 13%
- Other: 10.4%

**Outbound Unit-level:**
- Cloud: 16%
- Cloud (Chain): 12.8%
- Cloud: 18%
- Cloud: 27%
- Cloud: 21.6%
- Cloud: 26%
- Cloud: 20.8%
- Cloud: 100%

**Dispenser/Pharmacy (Chain):**
- Outbound Unit-level: 14.4%
- Outbound Unit-level: 27%
- Outbound Unit-level: 21.6%
- Outbound Unit-level: 26%
- Outbound Unit-level: 20.8%
- Outbound Unit-level: 100%

**Hospital:**
- Outbound Unit-level: 100%

**Figure 13b - Most Likely Scenarios**
In order to estimate the total costs of the combined system integration and aggregation
Furthermore, as serialization is gradually introduced into the US pharmaceutical ecosystem, incidences of verification errors can be expected to occur with relative frequency. This is due purely to learning curves and will most likely decrease as processes and systems are tweaked to bring them into alignment. However, preparation should be undertaken to process all the potentially quarantined product to ensure that no shortages occur due to information mismatches.

5.2 Implications

The implications of this study are primarily threefold: 1. Serialization following a Centralized data model will result in significantly higher costs, but will offer a more robust and secure solution. 2. Working capital can be expected to increase in any scenario, though scenarios employing a Matroyshka relational model will see a smaller increase in working capital over time than those employing a Unit Level relational model. 3. High data sharing and storage requirements will make database management a significant challenge – to achieve optimum database resiliency and efficiency, it may be expedient to employ an outside party to manage this portion of the serialization process.

1. A Centralized data model offers many advantages in terms of data reliability, database robustness, and ease of management. It is also the most scalable data model option. However, the immense costs necessary to create a reliable and scalable Centralized data model may discourage existing industry players to invest in this capability.

2. Working capital throughout the pharmaceutical industry can be expected to increase. The rise in inventory will comprise both a temporary increase (primarily due to inventory prebuild necessary to counterbalance line down time resulting from equipment installation) and a more permanent increase caused by the elongation of shipping and
receiving processes (increased cycle time). Any scenarios employing a Matryoshka relational model can expect to see a lower increase in long-term inventory due to the aggregation of data in nested linked-pedigrees, while Unit Level relational model scenarios will see longer cycle times and higher inventory levels.

3. Higher data requirements, necessitating redundant information systems and resilient networks, will be needed as a result of serialization requirements. The sharing and verification of serial numbers across multiple players in the value chain is expected to pose a serious challenge for the coming years. For this reason, employment of an outside party with expertise in database management could be a potential option that would both increase information reliability as well as reduce the up-front investment necessary for creating a Centralized data model.

4. Number of errors for unit-level and matryoshka variables:

Unit-level – volume of work is large therefore it is harder to scan everything correctly.

Matryoshka – the wrong pallet would be sent to the customer (or the customer packaging is mismatched).

Chapter 6: Conclusion

When looking at the impact of serialization on the US pharmaceutical industry, we have identified several key trends: 1. A need for higher level investment in information system resiliency and redundancy, 2. An increase in working capital across the board, but most saliently in scenarios involving a Unit Level relational model, and 3. The growing ability of 3rd Party data management service providers to offer a valuable solution to the immense data manipulation and storage requirements posed by DSCSA.
These impacts are expected to have long lasting consequences on all players in the pharmaceutical industry, and may pose difficulties to any new companies trying to enter the market. However, due to auspices of the DSCSA impacting only key activities in drug tracking and tracing, many auxiliary players in pharmaceuticals (3PLs, for example) may find themselves exempt from the rulings and free to continue business as usual.

Nevertheless, serialization is here to stay, and the implementation of a proper track & trace system for all pharmaceuticals will take a disciplined and rigorous approach. Pharmaceutical firms could give themselves the best chance to successfully implement serialization by using best practices proposed by the likes of Davison and Laskowski, as well as leveraging lessons from overseas. Any efforts would need to account for the needs of both downstream and upstream customers; furthermore, the serialization technology will need to be easily scalable and resilient to malicious attacks.

At the same time, government regulations containing a higher degree of specificity around responsibility and accountability would help improve any effort towards implementing either a Centralized or Decentralized database. Guidance around the maintenance of a “single source of truth”, and specifications around the data format would both serve to reduce the level of uncertainty existing in the industry around appropriate Serialization standards.

Although this thesis was completed with great attention to accuracy of information, some limitations do exist:

- Pharmaceutical industry figures may not be completely accurate, and hence, the financial impacts mentioned are directional in nature and should be recalculated with company specific data if possible.

- Technological recommendations as to which systems (GS1, QR codes, 2D barcodes) should be used for serialization have not been made in this thesis due to the technical and political nature of this decision. Further clarification on this topic should ideally come from the FDA.
- Process diagrams, both current state and future state, are meant as examples only. The process could differ for different companies depending on their specific situation and needs.

- Implications for the pharmaceutical industry, as stated above, apply only to the immediate years after completion of DSCSA (2023). It is likely that incremental advances in both process and technology would negate any increases in cycle time and inventory caused by serialization before the 10-year estimated time frame.

- The costs of capital expenditures are based on average industry equipment estimates. These figures should be adjusted appropriately for volume and capability before using stated costs for capex estimates.

- Due to the lack of historical data (and empirical data from overseas serialization attempts), the magnitude of the impact of serialization is difficult to determine. Suffice it to say, the forecasted impact of serialization is directionally correct.
APPENDIX 1 – Comparison of Centralized and Decentralized, Matroyshka vs Unit Level Scenarios

Relative Cost Comparison of each Scenario – Costs normalized to universal baseline

<table>
<thead>
<tr>
<th>Data Model</th>
<th>Relational Model</th>
<th>IT Investment</th>
<th>Operating Cost</th>
<th>CAPEX</th>
<th>Net Present Cost - 10 Year Recurring</th>
<th>Net Present Cost - 10 Year Recurring</th>
<th>Net Present Cost - 10 Year Recurring</th>
<th>One time Investment</th>
<th>Net Present Cost - 10 Year Recurring</th>
<th>Relative 10 year cost - Normalized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Centralized (3rd party)</td>
<td>Matroyshka</td>
<td>1.0x</td>
<td>54.8x</td>
<td>12.0x</td>
<td>6.7x</td>
<td>54.0x</td>
<td>195%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Centralized (3rd party)</td>
<td>Unit Level</td>
<td>1.0x</td>
<td>54.8x</td>
<td>14.8x</td>
<td>5.9x</td>
<td>54.4x</td>
<td>196%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Centralized (Manuf)</td>
<td>Matroyshka</td>
<td>13.4x</td>
<td>14.8x</td>
<td>12.0x</td>
<td>6.2x</td>
<td>46.8x</td>
<td>167%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Centralized (Manuf)</td>
<td>Unit Level</td>
<td>13.4x</td>
<td>14.8x</td>
<td>14.8x</td>
<td>9.9x</td>
<td>46.8x</td>
<td>169%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Centralized (Govt.)</td>
<td>Matroyshka</td>
<td>1.0x</td>
<td>34.4x</td>
<td>12.0x</td>
<td>6.2x</td>
<td>53.6x</td>
<td>193%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Centralized (Govt.)</td>
<td>Unit Level</td>
<td>1.0x</td>
<td>34.4x</td>
<td>14.8x</td>
<td>9.9x</td>
<td>54.1x</td>
<td>195%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decentralized</td>
<td>Matroyshka</td>
<td>7.5x</td>
<td>2.5x</td>
<td>12.0x</td>
<td>6.2x</td>
<td>27.7x</td>
<td>100%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decentralized</td>
<td>Unit Level</td>
<td>7.5x</td>
<td>2.5x</td>
<td>14.8x</td>
<td>9.9x</td>
<td>18.2x</td>
<td>102%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Net Present Cost

Relative Costs (10 Year Horizon)
### 10-year Horizon Relative Net Present Cost Comparison – Costs normalized by row

<table>
<thead>
<tr>
<th>Data Model</th>
<th>Relational Model</th>
<th>IT Investment</th>
<th>Operating Cost</th>
<th>CAPEX</th>
<th>Net Present Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Centralized (3rd party)</td>
<td>Matryoshka</td>
<td>2%</td>
<td>64%</td>
<td>22%</td>
<td>12%</td>
</tr>
<tr>
<td>Centralized (3rd party)</td>
<td>Unit Level</td>
<td>2%</td>
<td>64%</td>
<td>27%</td>
<td>7%</td>
</tr>
<tr>
<td>Centralized (Manuf)</td>
<td>Matryoshka</td>
<td>29%</td>
<td>32%</td>
<td>26%</td>
<td>13%</td>
</tr>
<tr>
<td>Centralized (Manuf)</td>
<td>Unit Level</td>
<td>29%</td>
<td>32%</td>
<td>32%</td>
<td>8%</td>
</tr>
<tr>
<td>Centralized (Govt.)</td>
<td>Matryoshka</td>
<td>2%</td>
<td>64%</td>
<td>22%</td>
<td>12%</td>
</tr>
<tr>
<td>Centralized (Govt.)</td>
<td>Unit Level</td>
<td>2%</td>
<td>64%</td>
<td>27%</td>
<td>7%</td>
</tr>
<tr>
<td>Decentralized</td>
<td>Matryoshka</td>
<td>25%</td>
<td>9%</td>
<td>43%</td>
<td>22%</td>
</tr>
<tr>
<td>Decentralized</td>
<td>Unit Level</td>
<td>25%</td>
<td>9%</td>
<td>53%</td>
<td>14%</td>
</tr>
</tbody>
</table>
APPENDIX 2 – Industry suggested RFQ questions for serialization implementation and supplier selection

Industry prep
- Outline the differences between old and new process, one-time and ongoing costs difference.
- What will your standard information system architecture look like for hardware and software?
- Have you accounted for backup and recovery capability? Are you engaged with cloud capability or local servers?
- How have you interpreted the standards for interoperable data exchange, and the legislative and regulatory requirements, and are they consistent with everyone in your supply chain?
- Have you coordinated with all of your trading partners and your CMOs?
- What are your budgetary and schedule constraints?
- Do you have the resources available to implement your enterprise-wide program?
- How will serialization impact your line efficiency, operations, and distribution?
- Does your current label or carton artwork accommodate the area required for printing of serialized information?
- What is your interpretation for an aggregation strategy – DSCSA does not require it for 2017, but will downstream trading partners interpret it differently and/or require it to manage their business processes and/or be in compliance?
- How do you plan on handling rework/returns and exceptions?

Supplier RFQ questions
- How informed is the partner with current regulatory requirements? This is important to ensure red functionality is available in the solution and also ensures that the partner will be a valuable contributor in longer term strategic initiatives.
- Is the partner able to supply solutions using tried and trusted components and technologies already in use in your production line? This will save considerable integration costs and time.
- Has the partner demonstrated the performance needed to meet the requirements?
- Does the partner have the financial stability and resources to meet near-term requirements and to deliver an economical service in the long-term?
- Does the partner have global service and support strategically located for rapid response when needed on site?
- Does the partner solutions have the flexibility to integrate your current software and hardware requirements including the ability to incorporate new features as technology and requirements evolve?
<table>
<thead>
<tr>
<th>Row Labels</th>
<th>Column Labels</th>
<th>Sum of Total Cost</th>
<th>Sum of Per Indiv.</th>
<th>Total Sum of Total Cost</th>
<th>Total Sum of Per Indiv.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Matryoshka Unit-level</td>
<td>Matryoshka Unit-level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dispencer/Pharmacy</td>
<td>$</td>
<td>-</td>
<td>$</td>
<td>$</td>
<td>$</td>
</tr>
<tr>
<td>Independent Dispenser/Pharmacy</td>
<td>$</td>
<td>-</td>
<td>$</td>
<td>$</td>
<td>$</td>
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<tr>
<td>Manufacturer DC</td>
<td>$</td>
<td>158,060,000</td>
<td>$</td>
<td>46,770,000</td>
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<tr>
<td>Manufacturer Facility</td>
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<td>841,203,602</td>
<td>$</td>
<td>856,628,952</td>
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<tr>
<td>Repackager</td>
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<td>74,750,000</td>
<td>$</td>
<td>46,000,000</td>
<td>$</td>
</tr>
<tr>
<td>Self Dispensing DC</td>
<td>$</td>
<td>-</td>
<td>$</td>
<td>-</td>
<td>$</td>
</tr>
<tr>
<td>Wholesaler</td>
<td>$</td>
<td>76,150,000</td>
<td>$</td>
<td>46,000,000</td>
<td>$</td>
</tr>
<tr>
<td><strong>Grand Total</strong></td>
<td><strong>$</strong></td>
<td><strong>1,150,163,602</strong></td>
<td><strong>$</strong></td>
<td><strong>996,168,952</strong></td>
<td><strong>$</strong></td>
</tr>
<tr>
<td>Manufacturer</td>
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<td>999,263,602</td>
<td>$</td>
<td>903,398,952</td>
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</tr>
<tr>
<td>Safety Stock for 0.5 day machinery</td>
<td>$</td>
<td>745,288,194</td>
<td>$</td>
<td>745,288,194</td>
<td>$</td>
</tr>
<tr>
<td>installation time</td>
<td>$</td>
<td>-</td>
<td>$</td>
<td>-</td>
<td>$</td>
</tr>
<tr>
<td>Manufacturer less SS</td>
<td>$</td>
<td>253,975,408</td>
<td>$</td>
<td>158,110,758</td>
<td>$</td>
</tr>
</tbody>
</table>

APPENDIX 3 – CAPEX costs per echelon
APPENDIX 4 – Inbound log information requirements

Inbound Log
Fill in the following info:

<table>
<thead>
<tr>
<th><strong>Serial Number</strong></th>
<th>12345678qwerty</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Child Serial Numbers</strong></td>
<td>12345678qwerty1</td>
</tr>
<tr>
<td><strong>Child Serial Numbers</strong></td>
<td>12345678qwerty2</td>
</tr>
<tr>
<td><strong>Child Serial Numbers</strong></td>
<td>12345678qwerty3</td>
</tr>
<tr>
<td><strong>Child Serial Numbers</strong></td>
<td>12345678qwerty4</td>
</tr>
<tr>
<td><strong>Child Serial Numbers</strong></td>
<td>12345678qwerty5</td>
</tr>
<tr>
<td><strong>Child Serial Numbers</strong></td>
<td>12345678qwerty6</td>
</tr>
<tr>
<td><strong>Lot number</strong></td>
<td>123</td>
</tr>
<tr>
<td><strong>National Drug Code and Electronic Product Code</strong></td>
<td>98</td>
</tr>
<tr>
<td><strong>Manufacturer</strong></td>
<td>GSK</td>
</tr>
<tr>
<td><strong>Product Type</strong></td>
<td>A</td>
</tr>
<tr>
<td><strong>Quantity</strong></td>
<td>30 ml</td>
</tr>
<tr>
<td><strong>Dosage form</strong></td>
<td>15ml</td>
</tr>
<tr>
<td><strong>Strength</strong></td>
<td>xx</td>
</tr>
<tr>
<td><strong>Product Name</strong></td>
<td>AAA</td>
</tr>
<tr>
<td><strong>Expiration Date</strong></td>
<td>5/3/20</td>
</tr>
<tr>
<td><strong>Supplier Name</strong></td>
<td>GSK</td>
</tr>
<tr>
<td><strong>Supplier Location</strong></td>
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</tr>
<tr>
<td><strong>Lot number</strong></td>
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<tr>
<td><strong>Product Expiration Date</strong></td>
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</tr>
<tr>
<td><strong>Quantity</strong></td>
<td>123 units</td>
</tr>
<tr>
<td><strong>Transaction Date</strong></td>
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</tr>
<tr>
<td><strong>Shipping Date</strong></td>
<td>10-Mar-17</td>
</tr>
<tr>
<td><strong>Invoice Number</strong></td>
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</tr>
<tr>
<td><strong>PO Number</strong></td>
<td>9876544h</td>
</tr>
<tr>
<td><strong>Product Owner</strong></td>
<td>Company Name: CVS</td>
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<tr>
<td><strong>Location ID</strong></td>
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</tr>
<tr>
<td><strong>Data Owner</strong></td>
<td>Company Name: e.g. Tracelink</td>
</tr>
<tr>
<td><strong>Person Name assigned</strong></td>
<td>John Smith</td>
</tr>
<tr>
<td><strong>Transfer History</strong></td>
<td>All previous transactions document to be uploaded</td>
</tr>
<tr>
<td><strong>Date of transfer of ownership</strong></td>
<td>Upload</td>
</tr>
</tbody>
</table>
APPENDIX 5 – Assumptions for Capex one-time costs

In order to estimate the whole industry wide initial capital requirements we have constructed the tree of all the costs that are applicable for the change. These costs relate to

- Line upgrade for **serialization**, 
- Additional **inbound** equipment, 
- Additional **outbound** equipment.

Serialization is assumed to be applicable to Manufacturer’s Facility and DC. It does not apply to Wholesaler as 97% of the product is dispatched in the unit-level bases, hence does not require to create extra serial numbers.

Matryoshka approach applies to Manufacturer and Wholesaler. Assume for upstream supply chain it is all just unit-level.
Line upgrade for serialization includes:

- Integrated unit level serialization equipment
- Installation costs of the serialization equipment
- Vision Equipment
- System integration of vision software and hardware for the serialization and vision equipment
- Checkweighing equipment/Scanner/Camera
- System integration of software and hardware for checkweighting equipment
- Equipment usage training
- Factory size increase and preparation to accommodate the equipment
- Label redesign and FDA Supplemental New Drug Application (sNDA) approval
- Safety stock (Inventory holding) for installation time – NOT accounted as part of the CAPEX

Additional inbound equipment includes:

- De-casing Equipment
- Scanning/Vision Equipment
- Installation costs

Additional outbound equipment includes:

- Aggregation equipment
- Equipment installation costs
- Warehouse storage increase due to increased inventory
- Equipment usage training
- Project management for installation
BIBLIOGRAPHY


