Utilizing Unit-Level Tracking Technology to Strengthen the Pharmaceutical Supply Chain and Combat the Opioid Epidemic

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On my honor as a student, I have neither given nor received any unauthorized aid on this assignment.

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Acronyms

DSCSA:
Drug Supply Chain Security Act of 2013

CDC:
Centers for Disease Control

FDA:
Food and Drug Administration

OMB:
Office of Management and Budget

PMPs:
Prescription Monitoring Programs

PV:
Present Value

RFID:
Radio Frequency Identification

US:
United States

VSL:
Value of a Statistical Life

2D:
Two-Dimensional

Executive Summary

The opioid epidemic in the United States generates societal costs exceeding $500 annually (Council of Economic Advisers, 2017). Drug diversion, or the illegal funneling of prescription drugs from legal sources to an illicit market, occurs throughout the pharmaceutical supply chain (Bell, 2010; Hall and Degenhardt, 2007; Inciardi et al., 2007; Institute of Medicine, 2013; Katz et al., 2007; Surratt et al., 2014). Diversion is driven by two primary weaknesses in the distribution process. First, opioids are too at accessible at the end of the supply chain due to physician overprescribing and patient resale. Second, theft and counterfeiting occur at intermediary points throughout the shipping process. This type of diversion is difficult to prevent because data analyzing a package's trip through the supply chain is rarely collected and centralized for research. Regulators and consumers have long demanded a more secure supply chain capable of tracking and monitoring goods throughout the distribution chain to quell these issues.

On November 27, 2013, Congress passed the Drug Supply Chain Security Act (DSCSA). The law called for the Food and Drug Administration (FDA) to construct a national electronic track-and-trace system for prescription drugs in the US by 2023 to reduce drug diversion and protect consumers (FDA, 2017). Track-and-trace programs monitor the movement of goods through a supply chain using tracking technology attached to each individual product. The tracking units carry data identifying the product, such as a unique serial code, and are scanned at each point in the supply chain, mapping the trajectory of packages as they are shipped (Coustasse, 2016). Data on every package is centralized to identify weaknesses in the supply chain where products are commonly diverted. As part of the FDA's 10-year implementation plan, deadlines have been set for private stakeholders in the pharmaceutical supply chain, namely manufacturers, wholesalers, and dispensers or pharmacies, to ensure compliance (Drug Safety Project, 2014; Mixter, 2017). One of the first actions stakeholders must take is to integrate unit-level tracking into their existing processes.

This report provides IBM with three options to determine what course of action clients in the private sector should take to strengthen their supply chain, reduce the consequences of drug diversion on the opioid epidemic, and comply with the DSCSA. These options analyze different tracking options available to stakeholders as they respond to regulation:

- Option 1: Maintain Current Operations

- Option 2: Invest in Two-Dimensional (2D) Barcode Technology
- Option 3: Invest in Radio Frequency Identification (RFID) Technology

Each of these options are evaluated using four evaluative criteria: cost of tracking prescription opioids, cost-effectiveness, security, and sustainability. Based on projections analyzing these criteria, it is in IBM's best interest to recommend that clients in the private sector utilize 2D technology to comply with the DSCSA in the short-run, given its low cost and widespread familiarity among stakeholders. In the long-run, private stakeholders should switch to RFID tags once the price of the technology drops, as anticipated by experts based on trends in production (Coustasse et al., 2016). Data produced over time, quantifying the cost-savings in inventory management to suppliers participating in the US track-and-trace system, will also help determine when returns on additional RFID investment are worth the cost to private suppliers. The implementation portion of the report primarily addresses how stakeholders should determine when to transition from the short-run recommendation to the long-run recommendation.

The final section of the report offers further consideration on how other emerging technologies, specifically blockchain, could be utilized by the FDA to manage data in the pharmaceutical network. Research on blockchain indicates it could create significant savings in supply chain management as a highly effective data-sharing tool capable of securely recording and verifying transactions (Furlonger and Valdes, 2017; Kshetri, 2018). Blockchain was not included in options for private stakeholders for two reasons. First, it is not a unit-level tracking technology. It is a transaction monitoring system capable of gathering and organizing data, such as the data collected by prescription tracking units. Second, it is relatively new technology and has not been developed enough to utilize on such a large scale. That being said, the section offers steps forward for public stakeholders to assess the benefits of blockchain, evaluate small-scale applications of the technology, and anticipate potential barriers to its eventual application in the FDA's track-and-trace program.

Problem Definition

The amount of prescription opioid abuse in the United States is growing, contributing to a drug epidemic that costs the United States more than $500 billion annually (Council of Economic Advisers, 2017). Drug diversion in the supply chain generates expenses for stakeholders in the pharmaceutical industry and adds to the illegal market for prescription opioids. Responding to demands for a more secure supply chain, legislators passed the DSCSA in 2013, requiring the FDA to construct a track-and-trace program to track prescription drugs. As a result of the legislation, private stakeholders are now responsible for investing in the infrastructure needed to participate in the system. IBM must work with clients in the pharmaceutical supply chain and federal agencies to optimize technology-based solutions designed to reduce diversion.

This report will focus on technological tracking options available to private stakeholders participating in the track-and-trace system, then offer additional considerations on how the FDA could manage data collected as part of the program.

The Opioid Crisis

Societal Costs of the Opioid Epidemic

The opioid crisis has gained increased attention from policymakers in the United States due to its growing societal costs. These costs affect more than just the healthcare system, as fatalities from drug overdoses and expenses on the legal system continue to rise and impact the economy. Experts studying the opioid crisis have attempted to quantify these costs to convey the seriousness of the issue to lawmakers. For the sake of comparison, the following cost estimates have been converted to 2017 US dollars using the consumer price index (Bureau of Labor Statistics, 2018).

In 2001, a study conducted by Birnbaum et al. (2006) estimated that the societal cost of prescription opioid abuse in the United States was approximately $11.9 billion. When the same authors released another study in 2007, they found that the cost to society had risen to $63.6 billion, representing a substantial increase from six years prior (Birnbaum et al., 2011). A report released by The Council of Economic Advisers (2017) estimated that the societal cost of the opioid crisis in 2015 was approximately $514.7 billion, more than eight times greater than the 2011 estimate. The study differed from past analyses by calculating the cost of an opioid-related overdose using the "value of a statistical life," (VSL) instead of workplace productivity. The VSL is a tool commonly used by federal agencies in cost-effectiveness and benefit-cost analyses to compare the worth of different policy interventions. It is generally defined by how much individuals value different tradeoffs between wealth and mortality risk (Aldy and Viscusi, 2008). The study also improved on previous work by including the cost of illicit opioids, such as heroin, and adjusting for recent research indicating that opioid-related overdose fatalities are significantly underreported (Ruhm, 2017).

Although estimates of societal cost vary greatly depending on study design, it is clear that the opioid epidemic incurs substantial societal losses in the United States. While interventions designed to quell this issue are often focused on treatment and rehabilitation strategies, many believe that access to opioids is the root cause of this crisis. The following literature focuses on how drug diversion in the pharmaceutical supply chain is flooding U.S. markets with illicit opioid medication.

Contributing Factors

There are two primary factors contributing to the spread of opioids in the United States: consumer accessibility and diversion during the shipping process. In this instance, accessibility refers to the ability of individuals to obtain opioids, generally at the end of the supply chain, through patient resale or a doctor's prescription. Drug diversion, or the illegal funneling of prescription drugs from legal sources to an illicit market, also occurs at intermediary points during the shipping process, where drug packages are vulnerable to theft and counterfeiting (Surratt et al., 2014).

Consumer Accessibility

Ease of access is one of the primary reasons opioid abuse has become widespread in recent years. Despite a variety of factors contributing to the issue, domestic prescription rates are widely identified as a primary cause of the crisis (Dasgupta et al., 2018; Surratt et al., 2014; Hall and Degenhardt, 2017). Prescriptions for opioids in the United States peaked in 2012, when approximately 259 million prescriptions for opioid medications were distributed by health care providers, or "the equivalent of one for every adult in the country," (Rothstein, 2017). While many physicians prescribe opioids within the bounds of their intended use, the proliferation of "pill mills" demonstrates how the legal prescription of these drugs are contributing to their abuse (Kennedy-Hendricks et al., 2016; Surratt et al., 2014). Pill mills are clinics or facilities where health care providers prescribe large quantities of prescription drugs, often in exchange for cash, for both medical and non-medical reasons (Kennedy-Hendricks et al., 2016).

Pill mills have been identified as one of the primary sources of illicit medication in the black market. Evidence collected from methadone treatment programs in the United States from 1997 to 2008 suggests that doctors' prescriptions are one of the most common sources of prescribed opioids for abusers (Bell, 2010). Interviews with illegal drug dealers working in South Florida, conducted from September 2008 to August 2010, revealed that for 26 of the 50 participants, pain management clinics were the primary source of prescription drugs. Although a majority of interviewees reported no pain themselves, they claimed that "doctor shopping" for physicians and clinics with little to no examination or vetting system made acquiring the drugs easy (Rigg et

al., 2012). While prescription resale and pill mills are major sources of opioids in the United States, illegal activities also occur throughout the supply chain.

Drug Diversion during the Shipping Process

Drug diversion has plagued the pharmaceutical supply chain for decades (Bell, 2010; Inciardi et al., 2007; Institute of Medicine, 2013; Katz et al., 2007; Surratt et al., 2014; Hall and Degenhardt, 2007). The complexity and intricacy of the distribution chain makes it vulnerable to diversion at various points in the process. While prescription resale and pill mills have been identified as major contributors to the illegal market for these goods, diversion can also occur earlier in the distribution chain, as drugs are shipped from pharmaceutical manufacturers to licensed wholesalers and pharmacies (Katz et al., 2007). Due to difficulty tracking and monitoring these goods during shipping, there is limited data on the amount of medication diverted each year, particularly because some of these goods are funneled back into the legal supply chain (Inciardi et al., 2007; Institute of Medicine, 2013; Katz et al., 2007).

Despite the challenges associated with tracking drug diversion, some studies have attempted to provide estimates. A study analyzing reports of pharmaceutical supply chain losses using DEA data from 2000 to 2003 found that approximately 28 million dosage units were stolen through pharmacy robberies in that time span (Katz et al., 2007). Thefts occurring earlier in the supply chain often yield even greater quantities of drugs. In 2010, more than $75 million worth of medicine was stolen from an Eli Lilly warehouse in Connecticut. Global Threat Assessment, FreightWatch International, a supply chain security company, claims that the theft of pharmaceuticals in the United States increased by 283 percent from 2006 to 2008 (Institute of Medicine, 2013). Diversion of opioid medication incurs substantial costs on pharmaceutical companies and contributes to the illegal market for these goods. Regulators and consumers have long demanded a more secure supply chain capable of tracking and monitoring goods throughout the distribution chain. The following section describes some of the interventions initiated in response to this problem.

Interventions

State Model: Prescription Monitoring Programs

Prescription monitoring programs (PMPs) are state level interventions designed to track the prescription of federally controlled substances. Programs are typically overseen on the state level by a designated agency, most commonly the state's Board of Pharmacy or Department of Health. Funding comes from grants authorized as part of the Harold Rogers Prescription Drug Monitoring Program and the National All Schedules Prescription Electronic Reporting Act (Paulozzi et al., 2011). Drug package data collected as part of these programs generally includes the prescriber, dispenser, patient, drug, dose, and the amount dispensed. The data is then centralized and made accessible to practitioners and pharmacists, although some states allow law enforcement, regulatory boards, and research organizations to also analyze findings (PDMPTTAC, 2017). Currently, 49 statewide PMPs exist in the United States, in addition to programs in the District of Columbia and Guam (2017).

PMPs are point-of-dispensing monitoring systems. Data is exclusively collected from retail pharmacies and other dispensers, strictly focusing on the transaction from dispenser to patient at the end of the supply chain (Vella, 2013). Over time, PMPs have faced criticism for failing to efficiently integrate their findings in health information technology (HIT) systems and for not using their data to address issues (Division of Unintentional Injury Prevention, 2017; Paulozzi et al., 2011). The effectiveness of these programs remains unclear, some literature going as far as to suggest that they are associated with more, "than a 30 percent reduction in the rate of prescribing Schedule II opioids," while others identify no significant relationship (Bao et al., 2016; Division of Unintentional Injury Prevention, 2017; Reifler et al., 2012). Inconsistent findings are at least partly due to variation in regulation and reporting rules for PMPs in different states.

National Model: Track-and-Trace Programs

Another tool used to monitor drug distribution channels are track-and-trace programs. While they operate similarly to PMPs, collecting and centralizing prescription data on federally controlled substances, track-and-trace programs tend to operate on a larger scale than PMPs, which are generally restricted to the state level. With track-and-trace, drugs are monitored from

the beginning of the supply chain, starting with the manufacturer, to the end, finishing with the prescriber and patient (Institute of Medicine, 2013). For that reason, track-and-trace programs not only gather data on the distribution of federally controlled substances, but also increase accountability and transparency for manufacturers, wholesalers, and dispensers throughout the drug supply chain. Systems on the state level, typically point-of-dispensing programs, are able to "track" a drug, but fail to "trace" the drug's path back to its origin. Track-and-trace programs are able to do so by creating a documented roadmap of transactions (Rodgers, 2010).

Track-and-trace systems rely on serialization, where every product is given a unique identification code that is used as a distinguisher. Individual serial codes are stored using tracking technology, typically at the unit-level using either a barcode, RFID tag, or mobile verification scratch-off code (Barlas, 2011; California State Board of Pharmacy, 2008; Institute of Medicine, 2013; Traynor, 2011). While track-and-trace programs have the potential to greatly reduce drug diversion and strengthen the pharmaceutical supply chain, they are relatively new and complex systems that place additional demand on supply-side stakeholders. Implementing a nationwide program would require manufacturers, wholesale distributors, and dispensers to make major changes to their existing processes (Institute of Medicine, 2013).

Although untested in the United States on the national level, prescription track-and-trace programs have been adopted by foreign governments in recent years. Sweden launched a pilot program in September 2009, placing 2D barcodes with unique serial identifiers on 95,000 drug packages. They found that once pharmacies were equipped with the scanners needed to identify codes, the verification process was smoothly integrated in the workflow. Turkey, Brazil, and France also require serialization codes on drugs leaving manufacturers or coming into their countries (Barlas, 2011). While these programs add transparency to the drug distribution process, the costs associated are often quite high.

Track-and-trace programs incur costs throughout the pharmaceutical supply chain. For a drug to be properly tracked through the entire shipping process, every stakeholder must be equipped with the technological infrastructure needed to scan and process packages. Comprehensive programs require significant alterations to existing manufacturing and warehousing management systems. For example, often cases must be opened and reopened for scanning and verification, taking time and creating expenses beyond the equipment costs for intermediaries. On the more local level,

track-and-trace programs ask far more of pharmacies (Institute of Medicine, 2013). They require pharmacists to communicate with physicians and manufacturers. The demand on pharmacists is higher in track-and-trace programs than in point-of-dispensing systems because more stakeholders are involved in the verification process. The international scope of a comprehensive supply chain tracking system also comes with additional legal barriers and data regulations that vary across borders (Barlas, 2011). Critics of track-and-trace programs claim the systems are complex, plagued by feasibility concerns, and have not been evaluated enough to support given the high associated costs. Despite these concerns, US legislators support the idea and have tasked the FDA with developing the first national track-and-trace program monitoring prescription drugs.

Federal Legislation: The Drug Supply Chain Security Act (DSCSA) of 2013

Congress passed the Drug Supply Chain Security Act (DSCSA) on November 27, 2013, as part of the Drug Quality and Security Act. The law called for the FDA to construct a national electronic track-and-trace system for prescription drugs by 2023, aiming to reduce drug diversion and protect consumers. Although still in development, the system currently requires that all drug packages be identified using a standardized numerical identifier, similar to a serial code, and mandates that supply chain stakeholders comply with requirements related to product serialization, general product tracing, verification, and distribution security (Drug Safety Project, 2014).

The timeline for the project set three major deadlines for stakeholders in the supply chain (Drug Safety Project, 2014; Mixter, 2017).

- January 1, 2015: Manufacturers, wholesale distributors, and dispensers must have a system to capture, maintain, and provide transaction information.
- November 27, 2017: Manufacturers, wholesale distributors, and dispensers should be trained in their respective roles of placing, verifying, and accepting standardized numerical identifiers on drug packages. They also must be able to provide transaction information electronically, a first step toward an interoperable data system given some stakeholders still rely on hand-written records.

- November 27, 2023: Manufacturers, wholesale distributors, and dispensers must be able to participate in an interoperable electronic package-level traceability system to share and send information about transactions.

Despite these projections, implementation has been slow. The January 1, 2015, deadline had to be pushed back approximately 6 months and the FDA recently extended the deadline for manufacturers to print unique numerical identifiers on individual drug packages by a year to November 27, 2018. Drug distributors and pharmacists blame the FDA for moving too slowly to issue the necessary guidance for such an overhaul (Mixter, 2017). Members of the FDA claim that it takes time to unify data formats across a supply chain in which some participants use paper to record transaction information. Many doubt that the 2023 deadline will be met and question the interoperability of a national database given differences in training, methods, and standards of data collection across regions. The FDA has held a series of public meetings and workshops to gather input from experts working in the supply chain and determine what type of track-and-trace system will successfully integrate with the health care system and help curb the opioid crisis (Wechsler, 2017).

As part of these logistics, stakeholders must determine which tracking technology should be utilized at the unit-level. For the track-and-trace program to effectively monitor movement throughout the supply chain, each drug package must be equipped with a tracking unit carrying unique data. Track-and-trace systems tend to rely on either barcode, RFID, or mobile verification technology to fulfill this requirement. Although the FDA has thus far suggested manufacturers, wholesalers, and dispensers utilize 2D barcode technology to comply with regulation deadlines, agency officials are open to collaboration and continue to accept input from private stakeholders about how to optimize the new system.

Before adopting 2D barcode technology as part of the DSCSA, suppliers in the pharmaceutical supply chain must evaluate alternative options. Although relatively new, RFID technology offers innovative functionality in data collection due to its remote capabilities. Despite these benefits, the low price of barcode technology also makes it an appealing option. The FDA has created a rare opportunity for stakeholders to shape DSCSA regulations that will have a lasting impact on supply chains security and business operations. Any recommendation requires an understanding of the costs and effects associated with different unit-level tracking technologies.

Methodology

Drug diversion in the pharmaceutical supply chain is rampant, generating costs to suppliers and contributing to the opioid epidemic. A lack of transparency and accountability in the existing supply chain contributes to this problem. While previous prescription monitoring interventions were launched on the state-level, the FDA's new national track-and-trace program authorized as part of the DSCSA will significantly alter the pharmaceutical shipping process. The following section of this report will serve to identify and evaluate the options available to IBM's pharmaceutical clients best suited to enable unit-level drug tracking. These options are intended to curb the consequences of the opioid epidemic and limit costs to private stakeholders by reducing drug diversion. The next section describes criteria used to assess options, followed by a description and evaluation of each option. The report concludes with a recommendation and implementation considerations for private and public stakeholders as they prepare to launch the first national track-and-trace program monitoring prescriptions in the US.

Evaluative Criteria

When projecting outcomes associated with different tracking options, four main criteria were considered: cost of tracking opioid prescriptions, cost-effectiveness, security, and sustainability. While in most instances it is unnecessary to include both a cost and a cost-effectiveness criterion, each is needed for pharmaceutical distributors to understand the impact of different options on their potentially competing economic and societal interests. The DSCSA places the burden of implementation and compliance costs almost entirely on manufacturers, wholesalers, and dispensers, threatening to exclude those who fail to comply from the US drug market entirely (Infosys, 2017). Stakeholders are responsible for producing and equipping tracking units using their own resources. While IBM's pharmaceutical clients have an interest in curbing the opioid epidemic, justifying the inclusion of a cost-effectiveness criterion, their economic sustainability is also important. Although one option may be extremely effective in reducing opioid abuse, it's cost to stakeholders must be considered separately to evaluate the impact the option may have on business operations.

Cost of Tracking Prescription Opioids

Although the DSCSA requires that the vast majority of prescription drugs be regulated as part of the track-and-trace program, analysis for this criterion only considered costs associated with the tracking of opioid drug packages. The scope was narrowed to accurately portray how the cost of tracking opioid prescriptions compares to the impact those expenses have on the opioid crisis. Given that this report sought to reduce drug diversion as a means to aid in the opioid epidemic, the scope of costs must match the scope of the effect studied. Evaluating expenses based on all prescription drugs would disproportionately overrepresent costs, misleading private stakeholders by comparing the cost of tracking every prescription drug to the positive societal effect of monitoring exclusively opioid prescriptions.

This criterion measured the present value (PV) of costs for each option, discounted over a 10-year period at a 7 percent rate, as recommended by the Office of Management and Budget (OMB, 2003). A 10-year cost analysis was ideal, as implementation and production expenses are likely change over time due to advances in tracking technology (Coustasse et al., 2016). Cost calculations were split into two categories: variable and fixed. As reoccurring expenses, variable

costs were discounted over the 10-year period, whereas fixed costs were not because they were fully expensed in the first year. Fixed costs were one-time purchases needed for initial implementation. These purchases primarily consisted of the technological infrastructure, such as barcode scanners or RFID encoders, needed for private stakeholders to process different tracking units (RFID4U, 2017). Infrastructure requirements differed across options, requiring changes in estimates depending on the specific hardware and software needed.

Variable costs were annual expenses required for each option over the course of the 10-year analysis. Expenses were based on the total number of tracking units required annually and the additional labor needed to scan units at each point in the supply chain. The cost of tracking units was found by multiplying the price of one unit (e.g. a barcode) by the number of units required, where the quantity of trackers required equaled the number of opioid prescriptions in the United States in 2016 (CDC, 2017). The cost of labor was determined by the time taken for employees to scan and process different packages attached with trackers, varying greatly depending on what technology is utilized. The total number of hours spent processing units was found by multiplying the average time it takes an employee to scan an individual tracker by the number of trackers that require scanning each year. Multiplying the annual number of hours spent processing by the median wage rate of different employees in the supply chain resulted in the total labor costs.

Cost-Effectiveness

While the cost estimates for this criterion were drawn from the preceding analysis, the effectiveness of options in reducing opioid abuse was measured as their associated effect on the number of admissions to drug treatment centers in the United States. Therefore, the cost-effectiveness criterion measured the cost of one fewer admission to a treatment center associated with each option.

The effectiveness measure originated from a study by Dave et al. (2017) that found a significant association between state PMPs and substance abuse treatment admissions. While patients are often admitted to treatment centers for non-opioid related addiction issues, the study's results were suitable for this analysis because the effect on admissions was primarily driven by reductions in opioid abuse. Using a differences-in-differences framework, the authors isolated

the effect of monitoring programs based on timing of adoption across states. While previous studies offered little consensus on the effect of state PMPs, largely because regulations vary across legislatures, their study differed from past work by comparing the effect of programs in the eleven states where participation in the program was mandatory, as it will be in the future FDA system. The authors found that the mandatory PMP programs were associated with 5.8 fewer treatment admissions per 10,000 individuals ages 18 to 24.

While the scope of their finding limited effectiveness estimates used in this report to people ages 18 to 24, this is also the age demographic most affected by the opioid epidemic, making it a suitable group to study effects on abuse (2017). Although some foreign governments have already implemented track-and-trace programs on the national level and their results could have been used to project effectiveness domestically, major differences in healthcare systems abroad made the effect of state PMPs a better estimate for that of the United States' first federal program (Infosys, 2017). That being said, because the effect on treatment admissions is limited to a single age demographic and state PMPs are point-of-dispensing monitoring systems, as opposed to more comprehensive track-and-trace systems, it is safe to assume that the effectiveness measure used in this report is a conservative estimate of benefits associated with the FDA's track-and-trace program.

While this estimate provided a baseline to project the general effect of a national track-and-trace program on opioid abuse, further analysis was needed to differentiate how the estimate found by Dave et al. (2017) would change based on the unit-level tracking option utilized by stakeholders. Although there was little research directly comparing the effects of these technologies in the pharmaceutical industry, results from the retail industry, where businesses utilize unit-level trackers for inventory management, proved suitable to determine the relative effectiveness of options. Findings from retail applications of unit trackers, comparing inventory transparency for businesses after switching from one tracking technology to another, provided comparative data used to estimate the relative effectiveness of options (Advanced Mobile Group, n.d.). Detailed calculations on costs and effectiveness measures can be found in Appendix A and will be discussed further when evaluating the criteria of each option.

Security

The security criterion considered how well a policy enabled governing bodies to collect and protect private medical data. The ability to protect data from fraudulent behavior varied across different tracking technology platforms. Given the sensitive nature of pharmaceutical information, the ability of any legitimate or illegitimate party to falsify data was an important outcome measure. The criterion was measured on a subjective scale as either low, moderate, or high.

Sustainability

This criterion measured different options' future sustainability given long-term projections in the technological marketplace. Specifically, projections on how widely utilized a technology will be and how its price will change based on current trends. Given the scale and cost of the FDA's national tracing program, it was vital to consider how sustainable an option would be over time. The criterion was measured on a subjective scale as either low, moderate, or high.

Options

Private stakeholders in the pharmaceutical supply chain have three primary options to consider when selecting a tracking technology to comply with the DSCSA: maintain current operations, invest in 2D barcode technology, or invest in RFID technology. For the purpose of this analysis, alternative options, such as linear barcodes or mobile verification technology, were not considered because they were unable to store the amount of data required to participate in a comprehensive track-and-trace program.

Option 1: Maintain Current Operations

This policy option involves maintaining current business protocols, most likely resulting in the FDA eventually constructing a national track-and-trace system without input from valuable stakeholders in the private sector. Under this alternative, private stakeholders would not work with the FDA to define mutually beneficial regulations for the track-and-trace program, instead reacting to decisions made independently by public officials. The option leaves stakeholders vulnerable to regulation requiring a tracking technology that is costly, has limited data collection capabilities, or is ill-suited for the future of inventory management. Without collaboration between the public and private sector, it also seems increasingly unlikely that stakeholders will be able to comply with the 2023 goal set by the FDA.

Cost of Tracking Opioid Prescriptions

This cost criterion represents the incremental expense to supply-side stakeholders of tagging and tracking opioid prescriptions with one of the tracking technology options available. In this instance, incremental costs are not clear because pharmaceutical suppliers would not pre-emptively invest in any tracking technology, generating no new costs, instead continuing current operations and waiting until the FDA clearly defines what systems must be used to gather data. Under this option, technological compliance standards remain unclear until the FDA finalizes its guidance, making costs of the program uncertain and leaving suppliers vulnerable to agency decisions. Taking into account these considerations, the cost of tracking opioid prescriptions criterion is not applicable to this option.

Cost-Effectiveness

Measurements of cost-effectiveness are also not applicable to this option. Without proactive steps by pharmaceutical suppliers to choose and implement new tracking technology, there will be no positive effects on opioid abuse in the United States, at least until the FDA forces compliance. Failing to participate in the decision-making process leaves stakeholders unable to predict cost-effectiveness because it is unclear what tracking technology is preferable, particularly given differences in social and commercial interests.

Security

The pharmaceutical supply chain, as it exists today, is plagued by security issues. Shipments are stolen and counterfeited regularly, threatening the privacy and wellbeing of patients. When considering future outcomes, maintaining current operations is undesirable because the rate of drug diversion is high and continues to grow in the existing system (Institute of Medicine, 2013). Taking into account these considerations, the security measure for this option is low.

Sustainability

Current operations are ill-suited for the future given global trends in drug tracking technology. Improvements in data storage transmission have enabled unit-level tracking applications never seen before. Although still relatively new, drug tracking programs are becoming widespread. Policymakers in Argentina, Brazil, China, Colombia, India, Iran, the Philippines, Turkey, the EU, and the US have recognized the potential benefits and adopted some form of these systems (The World Health Organization, n.d.). The status quo is unsustainable as it becomes increasingly outdated and as policymakers in the US work toward a fully functional track-and-trace program by 2023. Taking into account these considerations, the sustainability measure for this option is low.

Option 2: Invest in Two-Dimensional (2D) Barcode Technology

Two-dimensional (2D) barcodes, also referred to as matrix barcodes, are capable of storing the necessary amount of information required by the track-and-trace program. Although similar in appearance, 2D barcodes differ from linear barcodes, such as those scanned on commercial goods at a grocery store, because they are capable of storing a greater amount of data (Institute of Medicine, 2013). By placing 2D barcodes on each drug package, regulatory agencies could identify and track individual serial numbers, expiration dates, and additional data required by the FDA. Intermediaries in the supply chain would scan the packages at each checkpoint, recording the transaction in the national database while also identifying any diversion in the shipping process. Turkey and Brazil already require 2D verification for drugs entering their respective countries as a way to monitor distribution.

Despite familiarity with this technology, barcodes come with some limitations. First, they can be forged and placed on packages anywhere during the supply process (Hemalatha and Rao, 2015). Second, data collection using barcodes places significant strain on every member of the distribution chain. If one of the many stakeholders handling a drug forgets to scan a product, its place in the supply chain becomes unclear and the information becomes worthless or misleading. While these codes are capable of being scanned by any camera or smartphone, they require line of sight identification, increasing the time burden of transactions on employees and the likelihood of mistakes (Institute of Medicine, 2013).

Cost of Tracking Opioid Prescriptions

A number of assumptions were built into the cost estimate for a national track-and-trace program utilizing 2D barcode technology. On the unit-level, suppliers would be responsible for producing a barcode to pair with every opioid prescription in the United States, totaling approximately 215 million prescriptions in 2016 (CDC, 2017). Each of those 2D barcodes would cost approximately $0.01 to produce according to market value (RFID4U, 2017). In addition to labor costs from producing and placing barcodes on drug packages, time spent by employees scanning packages as they move through the supply chain would also be included. Dividing the total number of barcodes produced annually, 215 million, by the average number of barcodes an employee can scan in an hour, approximately 209, resulted in the total number of labor hours stakeholders

would have to dedicate to scanning (Advanced Mobile Group, n.d.; Payscale, 2018). The total hours were then multiplied by the median wage rates of different employees in the pharmaceutical supply chain to determine annual scanning costs:

- Manufacturing Associate – $21.63/hour
- Production Associate (wholesale distribution) – $16.89/hour
- Pharmacy Technician – $13.78/hour

The PV of variable costs associated with barcode labels and labor, discounted over the 10-year analysis, was $400 million.

Stakeholders would also need to invest in the necessary infrastructure to process this technology, Specifically, they would need to purchase enough 2D scanners and industrial printers to produce and process 215 million barcodes. For manufacturers and wholesalers, estimates suggest at least one scanner and printer would be needed for every 1,000 prescriptions (RFID4U, 2017). For pharmacies, one scanner and printer would be required at every location in the US, so at about 67,753 pharmacies (Qato et al., 2017). Infrastructure costs differed for manufacturers, wholesalers, and pharmacies based on operations, but totaled approximately $1.7 billion. As a one-time expense, this cost was only incurred in year one.

Combining variable and fixed costs, the PV of costs for this option over a 10-year span was approximately $2.1 billion.

Cost-Effectiveness

The cost-effectiveness of the 2D barcode option was found using the cost estimates explained above and research conducted by Dave et al. (2017), claiming that mandatory PMP regulations were significantly associated with approximately 5.8 fewer admissions to rehabilitation centers per 10,000 individuals ages 18 to 24. Population projections over the course of the analysis estimate that the average number of people living in the United States ages 18 to 24 will be a little less than 31,000,000 annually (United States Census Bureau, 2017). Projecting the effect on treatment admissions for the entire age demographic, instead of for the 10,000-individual sample, indicates that the FDA's tracing program could result in approximately 17,800 fewer admissions to drug rehabilitation centers annually, or about 178,930 fewer admissions over the

span of the analysis. Dividing the option's cost of $2.1 billion by the total number of fewere admissions over 10 years, suggests that every $12,000 invested in the 2D barcode tracing program results in one fewer admission.

Security

2D barcodes offer moderate security because they are vulnerable to physical corruption, but safe from remote access to personal data. Barcodes can be produced on most standard printers, making them particularly susceptible to counterfeiting and copying (Institute of Medicine, 2013). Furthermore, their widespread use across different industries has made the infrastructure needed to scan and read codes common, increasing the likelihood that outside actors are capable of accessing pharmaceutical data (Advanced Mobile Group, n.d.). Although easily copied and produced, 2D barcodes are effective at protecting personal data from remote hacking. Technology that utilizes antennas to transmit data, such as RFID tags, can be remotely accessed and read, sometimes even altered depending on the specifics of the model, whereas barcode technology can only be physically corrupted because it is does not have the same capabilities. Taking into account these considerations, the security measure for this option is moderate because despite its weaknesses, it is still a significant improvement over the status quo.

Sustainability

2D barcodes are used heavily across different industries because they are cheap to produce and capable of storing more data than past unit-level technologies, such as linear barcodes. In the future, it is unlikely that the price of barcodes drops further given that it is already mass produced and in full demand. While it is unlikely that barcode technology is done away with in the next few decades, its technological limitations do not align with the future of data gathering. As unit-level tracking continues to improve and spread, products capable of remotely transmitting information will yield significant long-term benefits (Shin and Eksioglu, 2015). Shippers have a logical interest in being able to remotely check the quality of their goods in real-time that barcodes cannot meet. Barcode technology will not become obsolete in the near future, but its incompatibility with innovative data gathering methods limits its future sustainability. Taking into account these considerations, the sustainability measure for this option is moderate.

Option 3: Invest in Radio Frequency Identification (RFID) Technology

The most advanced tracking option currently available for the national track-and-trace program is radio frequency identification (RFID) technology. RFID tags are approximately the size of a grain of rice and can be used to carry unique electronic product codes on drug packages. They utilize small antennas to send and receive data stored on a chip (Coustasse et al., 2016). The chip can record information on a drug package's unique serial number, expiration data, batch code, and previous transactions. From the perspective of suppliers, one of the greatest benefits of RFID tags is that the data can be collected without attaining line of sight on each package, saving substantial time in logging transactions (Shin and Eksioglu; 2015). For the FDA, RFID tags are appealing because they store substantial amounts of data that can be accessed remotely. RFID applications in pharmaceutical tracking are relatively untested for two reasons. First, while innovative, RFID tracking requires significant technological infrastructure to participate in, something intermediaries in the supply process lack. Second, RFID tags are relatively expensive to purchase compared to other technological solutions, generating significant costs to private stakeholders (Hemalatha and Rao, 2015; Institute of Medicine, 2013). Based on technological requirements and high costs of implementation, RFID remains a policy option only in wealthy countries such as the United States.

Cost of Tracking Prescription Opioids

The cost estimate for the RFID option was found with many of the same assumptions used to estimate the cost of barcode technology. Variable costs, such as tag purchases and labor, were discounted over the 10-year span. For the purpose of this analysis, RFID tags were valued at $0.50 each based on the market price of the model most likely to be used by suppliers (RFID4U, 2017). Labor costs were once again determined using supply-side wage rates and the average number of tags that an employee was able to scan in hour, which in this case was 4,767 tags. RFID scan time made labor costs minimal due to savings in time from remote access. The PV of variable costs was approximately $770 million. Fixed costs were primarily made up of one-time infrastructure purchases needed to produce and scan RFID tags. Purchases included handheld code readers, fixed code readers, and printer encoders used to put data on tags (2017). The

number of handheld readers required was based on the number of pharmacies in the US, while the number of fixed readers and printer encoders was determined by the total number of prescriptions within the track-and-trace program (Qato et al., 2017; RFID4U, 2017). Even as a one-time expense, RFID infrastructure would cost private stakeholders approximately $2.7 billion to purchase.

Combining variable and fixed costs, the PV of costs over a 10-year span was approximately $3.5 billion.

Cost-Effectiveness

Cost-effectiveness for this option was determined using the previously discussed cost evaluation, and analysis on the relative effectiveness of RFID tags in ensuring inventory transparency when compared to barcode technology. When evaluating barcode technology's cost-effectiveness, 5.8 fewer admissions per 10,000 individuals was a reasonable estimate because it came from analysis of existing PMPs, which utilize present-day technology such as barcodes (Dave et al., 2017). As a relatively new technology in the pharmaceutical world, there was limited data on how RFID tags in drug tracking affect admissions to rehabilitation centers. However, studies on the effectiveness of RFID tags in commercial retail, where they are becoming popular inventory management tools, provided insight into their relative effects when compared to barcode technology. Companies switching to RFID inventory management systems, such as Wal-Mart, generally did so from previously utilized barcode systems, revealing the marginal benefits of one option over the other.

Analysis of Wal-Mart's inventory after switching to RFID tags showed that transparency increased approximately 35 percent (Advanced Mobile Group, n.d.). Assuming that inventory transparency improves supply chain security, the marginal benefits of a RFID tracking system to the supply chain would further reduce rehabilitation rates for treatment centers. If 2D barcodes were associated with 5.8 fewer admissions per 10,000 individuals, and RFID technology was 35 percent more effective than barcode technology in retail applications, then a track-and-trace system using the latter technology would reduce admissions by 7.8 per 10,000 individuals ages 18 to 24. Projecting the effect to the general population, RFID tags could result in about 24,000 fewer admissions annually, or about 240,000 fewer admissions over the 10-year analysis.

Dividing the option's cost of $3.5 billion by the total number of admissions prevented, indicates that every $15,000 invested in the RFID tag tracing program results in one fewer admission to a substance abuse treatment center.

Security

RFID technology has many comparative advantages in security over the preceding options. While barcodes are exclusively used for data storage, RFID tags have multiple capabilities and are programmable, allowing users to add encryption and passwords to prevent unwanted access (n.d.). These features are particularly important in the medical field, where doctor and patient privacy is prioritized. In addition to data protection capabilities, RFID tags offer physical security benefits as well. For example, an employee working in drug distribution could scan the barcode of a drug package then leave the building with the package, leaving only evidence that it disappeared somewhere in that segment of the supply chain. With RFID tags, antennas can transmit signals to nearby sensors, warning when a package is moved or opened preemptively (Shin and Eksioglu, 2015; Trepagnier, 2016). Although virtual access to data comes with an increased risk of hacking, advancements in sensor technology integrated with remote communication capabilities offer security benefits far beyond those of alternative options. Taking into account these considerations, the security measure for this option is high.

Sustainability

Early pharmaceutical applications suggest RFID technology extends far beyond geographical tracking. RFID tags can be used to collect a variety of data because of their unique ability to transmit information remotely through radio waves. For example, some retailers have monitored the temperature of packages by linking sensors to RFID tags, a quality assurance measure that could reduce liability and improve product recall efficiency. Sensors have also been used to track when a package or crate is opened in real-time, limiting and documenting diversion opportunities (Shin and Eksioglu; 2015). These applications could create substantial savings for private stakeholders in the supply chain when scaled to the pharmaceutical market. While these are retail examples, RFID tags are becoming increasingly widespread, ensuring that new functions continue to be explored as investors exploit their data transmission capabilities. Increased

production of RFID technology will also continue to drive down its price in the future (Coustasse et al., 2016). Taking into account these considerations, the sustainability measure for this option is high given its adaptive capabilities to future innovation.

Outcomes Matrix

	Cost of Tracking Prescription Opioids	**Cost-Effectiveness**	**Security**	**Sustainability**
Option 1: Maintain Current Operations	N/A	N/A	Low	Low
Option 2: Invest in Two-Dimensional (2D) Barcode Technology	$2.1 billion	$12,000 per reduction in treatment admissions	Moderate	Moderate
Option 3: Invest Radio Frequency Identification (RFID) Technology	$3.5 billion	$15,000 per reduction in treatment admissions	High	High

Recommendation

Short-Term Recommendation: Invest in Two-Dimensional (2D) Barcode Technology

Given the projected outcomes of each option, IBM should recommend that clients in the pharmaceutical supply chain utilize 2D barcodes as a means to comply with DSCSA deadlines in the near future.

The primary advantage that 2D barcode technology has over RFID technology is its price. As RFID infrastructure becomes increasingly popular, its price of production will drop. However, in the short-term, differences in costs criterion are significant. For the purpose of this analysis, RFID tags were valued at approximately $0.50, a conservative estimate for products sometimes ranging from $0.10 to $2.50 in price depending on the model and desired features (RFID4U, 2017). Even when using a conservative estimate, utilizing RFID tags to comply with the DSCSA at this time would generate approximately 66 percent more in costs than if stakeholders used 2D barcodes. Furthermore, sensitivity analysis indicated that the projected cost of RFID implementation used in this report would have to decrease by more than 40 percent before reaching a breaking point where this option is more affordable than 2D technology. RFID technology is exciting because it is relatively new and offers a variety of innovative applications across different industries, but because it is so new, there are questions about global standards and price projections that must be answered before stakeholders invest so heavily in this option to comply with the FDA's timeline.

When analyzing options available to those working in the pharmaceutical supply chain, time constraints impact decision-making. The FDA requires that private stakeholders have an electronic system in place to attach and verify numerical identifier codes on drug packages by November 27, 2018. 2D barcodes are the optimal choice for manufacturers and distributers trying to reach this deadline because they are familiar with the technology and it is affordable. Unlike RFID tags, 2D barcodes have globally agreed upon quality standards already in place, making the technology preferable in a large international venture with diverse regulations across different countries. Supply chain members are also likely to already have some of the technological infrastructure required to create, scan, and verify 2D barcodes, as they are commonly used across most industries, saving money on labor and infrastructure costs during implementation. Given volatility in the price of RFID technology and uncertainty surrounding

this relatively new tracking hardware, 2D barcodes are the preferred solution in the short-run for stakeholders working to meet the FDA deadline.

Long-Term Recommendation: Invest in Radio Frequency Identification (RFID) Technology

Based on long-term economic and technological trends, utilizing 2D barcodes to comply with the DSCSA's deadline, then investing in RFID tags in the future, offers numerous benefits to pharmaceutical suppliers.

Although RFID technology remains an option only for wealthy nations, economic trends suggest that in the future, it will cost a fraction of its current price. The price of RFID technology, while high, has been dramatically decreasing over time (2016). As it becomes an increasingly popular inventory management tool across different industries, production will continue to rise, decreasing costs and price as a result. Some compare the trajectory of RFID technology to that of solar technology, relatively expensive in early applications but cheaper as adoption became more widespread.

Waiting for implementation also allows private stakeholders time to fully evaluate the private benefits of participating in a track-and-trace program, such as cost-savings from improvements in distribution security and quality assurance practices, that are rarely assessed in socially driven research related to opioid abuse. Assuming technological trends continue, RFID will eventually be adopted by public and private stakeholders globally due to its advanced capabilities. As a result of increased adoption, global standards are likely to develop in the future as they did for 2D barcode technology, giving pharmaceutical suppliers a pathway to a RFID system that bypasses international regulatory complexities that could plague implementation if it were to occur today.

Implementation

The most important aspect of implementing this multi-step recommendation will be correctly identifying when stakeholders should switch from using 2D barcode trackers to RFID tags. Private sector stakeholders in the supply chain, such as manufacturers, wholesalers, and dispensers, are primarily interested in limiting costs during implementation. Their decision to switch from 2D barcode technology to RFID technology should be based on economic models projecting future returns, making it vital that they identify driving factors to monitor during implementation.

Anticipating Future Trends

The ideal time for pharmaceutical suppliers to switch from 2D barcodes to RFID tags will be primarily determined by economic and technological trends affecting cost estimates. Modeling these trends to project costs and benefits in the future will allow private stakeholders to accurately predict when the transition should occur based on long-term profitability. The greatest economic factor will be the price of RFID technology, such as that of tags, coders, and readers. Past trends and future projections suggest that as production of RFID technology increases, prices will drop, lowering the cost of implementation (2016). Based on technological trends, the cost-savings of RFID technology to suppliers will also grow over time.

In addition to changes in price, it is also important that private stakeholders quantify and model personal benefits over time not considered in this analysis. Advancements in tracking technology have created unforeseen benefits to commercial investors not considered when evaluating supply chain management systems in the past. Suppliers are now able to monitor product quality during the shipping process more efficiently than ever before due to advances in remote data access, sensor technology, and unit-level tracking (Durbin, 2017; Galer, 2017; Skin and Eksioglu, 2015). Technological advancements in tracking systems will not only improve public officials' ability to curb drug diversion, but also generate new inventory management benefits to private suppliers. This analysis utilized a cost-effectiveness criterion to evaluate how a national track-and-trace program may affect the opioid epidemic. Moving forward, a cost-benefit analysis that quantifies and compares monetary benefits to pharmaceutical suppliers from different tracking technology is necessary for suppliers to fully comprehend when they should switch from 2D barcodes to

RFID tags. Cost-savings enjoyed by suppliers as a result of improved inventory transparency and quality assurance must be included to accurately project the break-even point where suppliers are economically justified in switching tracking technologies.

Moving forward, private stakeholders must develop a predictive model to project when RFID implementation in the FDA's track-and-trace program is desirable given economic interests. Two primary functions should be at the core of the model. First, it should predict the price of RFID technology over time based on past pricing and production trends. Second, the model should quantify cost-savings to suppliers in the supply chain resulting from improvements in RFID and sensor technology, such as the ability to monitor specific aspects of product quality. In the near future, private stakeholders should comply with the DSCSA using 2D barcode technology, then develop a model that projects the return on investment of RFID technology based on changes in price and cost-savings over time. This model will predict when RFID technology inevitably becomes economically preferable to barcode technology so that stakeholders can make necessary preparations to implement change.

Barriers to Transition from Two-Dimensional (2D) Barcodes to Radio Frequency Identification (RFID) Tags

There are two primary obstacles that may impede private stakeholders' switch from 2D technology to RFID technology in the future: implementation cost and system compatibility.

Implementation Cost

Problem: The high initial investment cost associated with track-and-trace systems could deter private stakeholders from choosing multiple implementation options. Fixed costs paid in year one of the 2D barcode track-and-trace program make up approximately $1.6 billion of the $2.1 billion in costs over the 10-year project analysis. Given that suppliers are ill equipped to afford or apply RFID technology at this time, they may commit to barcode technology and be unwilling to switch in the future after paying the majority of costs upfront.

Potential Solution: While the upfront infrastructure needed to operate 2D barcode technology will be expensive to private stakeholders, they have little choice but to invest. 2D barcodes have

thus far been established as the minimum technological standard by the FDA and the deadline for suppliers is approaching, forcing companies to either comply or be removed from the market. When considering the long-term recommendation, it is important that private suppliers not over value sunk costs. As the price of RFID technology drops and supply chain security improves, reoccurring benefits over time outgrow one-time initial investments. Furthermore, some stakeholders are likely to already be equipped with at least some of the infrastructure needed to record transactions using barcode technology due to its popularity globally, further reducing upfront costs.

System Compatibility

Problem: While guidance explaining DSCSA regulations has recommended that 2D barcode technology be used to comply with data collection and storage standards, private stakeholders may face compatibility problems if they choose to utilize more advanced options, such as RFID technology, now or in the future. If drug manufacturers at the beginning of the supply chain choose to switch to RFID technology without first agreeing and coordinating with wholesalers and dispensers, tracking systems will vary greatly across stakeholders, making it difficult to collect and standardize data from different sources (Hemalatha and Rao, 2015).

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Potential Solution: There are two primary ways to overcome this compatibility issue. First, private stakeholders must collectively analyze technological trends and costs over time to fully comprehend the value that RFID technology will create in the future. Without a shared understanding of future potential, stakeholders will cling to the option that is currently cheaper. Second, they must be transparent and collaborate with one another to agree on unilateral action regarding major changes to tracking processes. Switching from one system to another as a group, preferably as a majority, will generate savings throughout the supply chain. If such collaboration proves unrealistic, then wholesalers and dispensers may be forced to at least develop data sharing systems capable of integrating different technologies used by manufacturers (Coustasse et al., 2016).

Further Considerations

The scope of this report was limited to options for private stakeholders seeking to improve supply chain security and comply with FDA deadlines. When considering the logistics of a national tracing program, certain topics were excluded from discussion because they were outside of the scope of tracking technologies. Data management by public stakeholders operating the program is another important issue that must be discussed moving forward. Although a relatively unexplored technology, blockchain offers significant benefits in data management. It could eventually be utilized by the FDA to organize and store data collected by RFID tags as part of the track-and-trace program.

While private stakeholders in the pharmaceutical supply chain face questions about how to best comply with FDA mandates, public sector employees overseeing implementation must decide how to best manage data collected as part of the new system. Although some DSCSA guidance has been released for manufacturers and dispensers seeking to comply with nearing deadlines, the FDA has yet to provide information on what database will be used to centralize information and, "is actively engaging stakeholders for input on options for the secure electronic, interoperable system," (Kshetri, 2018; Traynor 2011). Given the number of stakeholders that will be regularly submitting sensitive medical data as part of the track-and-trace program, it is vital that the FDA choose a database capable of securely recording transactions between parties while limiting costs. Blockchain technology merits serious consideration as an innovative, cost-savings solution.

Blockchain Background

Blockchain first became popular in the financial sector as a tool to legitimize cryptocurrencies, such as Bitcoin, so that users could cut costs and escape regulatory institutions. Blockchain is a "distributed ledger in which value-exchange transactions," are grouped into blocks that are chained to past blocks, or previous exchanges, creating an incorruptible record (Furlonger and Valdes, 2017). The technology was designed with three main characteristics in mind: decentralization, tamper-resistance, and strong authentication (Dai and Vasarhelyi, 2017). In its currency applications, blockchain has used a decentralized peer-to-peer model where all

members of a network have access to the transaction record, enabling them to verify and add to the ledger. Those within the network are unable to tamper with blockchain records because it is designed so that adding to the ledger requires massive computational resources (2017). The necessary computational resources come from a massive network of computers that each verify and record the transaction. Without consent from the majority of the network, computational costs make it nearly impossible for a party to tamper with blockchain records. The ledger is also secure from outside threats. Blockchain utilizes a "public-key cryptography," to accurately and reliably authenticate all party members, preventing imposters from infiltrating the system (2017). These characteristics give blockchain a secure infrastructure to enable reliable transactions between stakeholders, offering efficiency and security benefits that extend far beyond the financial sector.

As businesses continue to discover the benefits of blockchain, its popularity grows. Although originally invented to facilitate currency exchange online, many now realize that blockchain's applicability extends to other industries including healthcare, education, manufacturing and energy. A technology trends report published in 2017 by Gartner Predictions attempted to project a few of its future economic impacts (Furlonger and Valdes, 2017):

- By 2022: At least one innovative business built on blockchain technology will be worth $10 billion.
- By 2030: 30 percent of the global customer base "will be made up of things," and those things will use blockchain as a foundational technology with which to conduct commercial transactions.
- By 2025: The business value added by blockchain will grow to slightly over $176 billion, then surge as it becomes more widespread to exceed $3.1 trillion by 2030.

Blockchain in Supply Chain Management

Blockchain could revolutionize supply chain management across all industries by providing real-time, secure information between verified stakeholders in a network. By giving suppliers instant access to relevant data on the movement of their goods, blockchain cuts significant monitoring costs. For example, the food shipping process involves substantial product verification and quality assurance. The process is reliant on "manual verification and massive record keeping," a

reality in many modern shipping chains (Kshetri, 2018). As an electronic system, blockchain could significantly cut down on those costs while also while limiting food waste and ensuring the efficient removal of contaminated units using real-time data. The technology is well-suited to make an impact. Nir Kshetri identifies seven primary criteria of an effective supply chain: cost, quality, speed, dependability, risk reduction, sustainability, and flexibility. For each criterion, blockchain offers unique advantages to supply chain performance over past technologies (2018):

Supply Chain Criterion	Benefits of Blockchain
Cost	-Allows for specific and efficient recalls when necessary -Eliminates costs associated with paper record systems
Quality	-Provides data indicating the quality of goods during process -Identifies and removes sources of contamination easily
Speed	-Saves time on physical process by using digital system -Reduces need for communication and interaction between stakeholders
Dependability	-Verifies members of network using digital certification -Provides accurate data on product quality using digital measurement systems
Risk Reduction	-Limits transactions to only members of the network -Allows for credible verification of certain goods (e.g. fine wines) by experts reliably identified and accepted in the network
Sustainability	-Provides a clear image of stakeholders through identity verification -Offers data to improve processess and correct vulnurabilities
Flexibility	-Provides benefits in a variety of industrial supply chains -Gathers and stores diverse data types depending on stakeholder need

Barriers to Blockchain in Pharmaceutical Data Management

There are three primary obstacles that may impede the implementation of a blockchain system in the future: network access, public perception, and technological complexity.

Network Access

Problem: One of the defining features of blockchain systems is that they are decentralized in nature, with no single central authority. The structure prevents corruption by ensuring no single party can manipulate a transaction or data without consent from the majority of the network. The structure also enables any member within the network to view all transactions and data, a clear issue in the pharmaceutical industry given the sensitivity of medical information, particularly near the end of the supply chain when drugs are prescriptions to patients. Any blockchain system in the healthcare world would have to be able to protect user information and access within the network.

Potential Solution: If the FDA were to adopt this technology to manage data from the track-and-trace program, they could utilize permissioned blockchain to control the parameters of the network. The most common applications of blockchain, such as Bitcoin, are structured so that they are permissionless, allowing any individual to join the network and make transactions. Permissioned blockchain is a less well-known system format where a central authority invites members to a network and gives them authority to authorize parts of transactions (Dai and Vasarhelyi, 2017). The advantage of this system is that it prevents outside access to information and gives a central authority, such as the FDA, power over access to data within the network. The disadvantage of permissioned blockchain is that it involves fewer parties, requiring trust among those included in the network to not collude and manipulate data.

Technological Complexity

Problem: The next step forward in evaluating blockchain applications for the FDA's track-and-trace system is not entirely clear. The technology is still relatively new, generating many unanswered logistical questions about security and effectiveness. Public officials require evidence that both proves the benefits of blockchain in supply chain management and establishes a framework to build a scalable model.

Solution: Although still untested on the national scale, blockchain supply chain applications are being piloted in the private sector (Kshetri, 2018). Their findings will provide insights into cost-savings for businesses seeking to improve efficiency. For example, Maersk, the world's largest

container carrier, is currently working with IBM to test a blockchain program designed to reduce paperwork and fraud in international shipping. While this example is limited to commercial shipping, some of the initial pilot programs will also inform public stakeholders on effectiveness in healthcare applications. In San Francisco, the supply chain consultancy firm, LinkLab, recently collaborated with a blockchain startup called Chronicled, to launch a pilot track-and-trace program in the pharmaceutical industry in the hopes of developing a compliance model for the DSCSA. Companies like Modem and Gemalto are also exploring quality assurance capabilities, beyond simple location identification, that could be used in pharmaceutical tracking. They are working to collect and transmit real-time information on drug package conditions during shipping, such as temperature, humidity, and light conditions, using a blockchain system that saves time and paper costs (2018). This is the same type of data that RFID tags are uniquely equipped to collect and transmit remotely, showing how the two technologies could complement each other.

Public Perception

Problem: When considering the political feasibility of blockchain in the future, public perception is a key criterion. Blockchain is best known for its role in the rise of cryptocurrencies. Over time, it has become heavily connected to the successes and failures of currencies, such as Bitcoin, in the eyes of the public. As cryptocurrencies have become increasingly perceived as volatile and dangerous investments, skepticism of blockchain technology has risen.

Solution: Public and private stakeholders must be made aware of the distinction between cryptocurrency and blockchain. While cryptocurrency relies on blockchain to provide credibility and verifiability to the transaction process, blockchain does not require any form of cryptocurrency to operate. While this may be an obvious point to people familiar with the two technologies, for most, it is lost in a technical world outside the realm of common knowledge. As long as the public most closely associates blockchain with cryptocurrency, skepticism will remain. Educating the public and policymakers on the function of blockchain and highlighting positive returns from pilot applications in non-finance markets will be a first step toward removing the stigma.

Appendix A: Cost-Effectiveness Analysis Technical Appendix

The following appendix can be used to view additional details of calculations used in the cost-effectiveness calculations.

Baseline

The baseline to which policy options are compared is the status quo, where there are no costs or positive effects of a track-and-trace program. As of May of 2018, manufacturers, wholesalers, and pharmacies have not been forced to utilize a specific tracking technology by the FDA. Furthermore, the operational deadline for the FDA's program is 2023, suggesting that even once stakeholders choose and invest in a specific tracking technology, it may not be utilized until the network is fully developed.

Time Horizon and Discount Rate

The analysis is conducted over a 10-year time span beginning in 2023, the FDA's implementation deadline. Costs are discounted at a 7 percent discount rate.

Effectiveness and Cost Categories

Effectiveness is measured as the reduction in substance abuse treatment center admissions associated with each option. The criterion was limited to effects on individuals ages 18 to 24 based on available literature, but this was not particularly problematic given that this age demographic is the one most effected by the opioid crisis.

Cost categories are divided by fixed and variable costs. Fixed costs are one-time expenses at the beginning of implementation and therefore are not discounted. These costs primarily consisted of hardware needed to create or process different tracking systems, such as barcode scanners and RFID encoders. Variable costs were discounted over the 10-year analysis because they were annual expenses. This category included the cost of each tag attached to an opioid drug package, the labor to attach the tag, and the labor to scan each tag for manufacturers, wholesalers, and pharmacists.

General Assumptions

Assumption	Value	Justification/Source
Discount Rate	7%	Recommended by OMB[1]
Span of Analysis	10 years	Appropriate given rapid changes in technology over time
Number of Annual Opioid Prescriptions in the United States	215,000,000	2016 CDC Data[2]
Number of Pharmacies in the United States	67,753	Study tracking growth of pharmacies claims there were 67,753 in 2015[3]
Median Wage Rate of Manufacturing Associate	$21.63	Site collecting data on wage across industries[4]
Median Wage Rate of Production Operator	$16.89	Site collecting data on wage across industries
Median Wage Rate of Pharmacy Technician	$13.78	Site collecting data on wage across industries

[1] Office of Management and Budget, 2003
[2] CDC, 2017
[3] Qato et al., 2017
[4] Payscale, 2018

Average Number of Individuals Ages 18 to 24 in the US during span of analysis	30,850,000	Population Projections by the United States Census Bureau[5]
Baseline Reduction in Treatment Admissions per 10,000 Individuals ages 18 to 24 associated with Mandatory Prescription Monitoring Programs	5.8	Study finding significant relationship between mandatory PMPs and treatment center admissions[6]

Option 1: Maintain Current Operations

The inability to analyze the incremental costs of tracking opioids, or the subsequent effect tracking may have on opioid abuse, makes this option irrelevant to calculations explained in this section.

Option 2: Invest in Two-Dimensional Barcode (2D) Technology

Assumption	Value	Justification/Source
Reduction in Treatment Admissions per 10,000 Individuals Ages 18-24 associated with 2D Barcodes in Prescription Monitoring	5.8	Dave et al. study
Cost of a 2D Barcode	$0.01	Report comparing inventory tracking tools with a focus on barcodes, published

[5] United States Census Bureau, 2017
[6] Dave et al., 2017

		by RFID4U, a company that specializes in tracking technology consultation[7]
Number of 2D Barcodes Required	215,000,000	One for each opioid prescription
Cost of a 2D Barcode Scanner	$900.00	RFID4U estimate
Number of 2D Barcode Scanners Needed	215,000	Employees should own one barcode scanner for every 1,000 units that must be scanned[8]
Cost of an Industrial 2D Barcode Printer	$1,500	RFID4U estimate
Number of Industrial 2D Barcode Printers Needed	215,000	Employees should own one industrial printer for every 1,000 barcodes produced[9]
Number of 2D Barcodes Employees are able to Scan per Hour	209	Study on item-level tagging for retail operations[10]

Effectiveness

The effectiveness of a 2D barcode tracking system was calculated using findings from a study that determined mandatory state-level PMPs are associated with a 5.8 reduction in substance

[7] RFID4U, 2017
[8] Ibid
[9] Ibid
[10] Advanced Mobile Group, n.d.

abuse treatment admissions per 10,000 individuals ages 18 to 24 (Dave et al., 2017). Although the logistics of programs vary from state to state, barcode technology accounts for the vast majority of the unit-level tracking market, making it reasonable to assume that the findings reflect the capabilities of 2D barcodes. The effectiveness measure was then projected from the 10,000 person sample population to the overall population of individuals ages 18 to 24 using the following formula:

Reduction in Treatment Center Admissions for Individuals Ages 18 to 24 in the US

= Total Number of Individuals Ages 18 to 24 in the US ÷ Population Sample Used in Study × Effect on Population Sample Found in Study

= 30,850,000 ÷ 10,000 × 5.8

Effectiveness calculations suggest a 2D barcode tracking program will result in 17,893 fewer treatment admissions annually, or approximately 178,930 fewer over the 10-year analysis.

Fixed Costs

The following formula was used to calculate fixed costs:

Technological Infrastructure Costs

= (Number of 2D Barcode Scanners Needed × Price of a 2D Barcode Scanner) + (Number of Pharmacies in the US × Price of a 2D Barcode Scanner) + (Number of 2D Industrial Barcode Printers Needed × Price of an Industrial 2D Barcode Printer) + (Labor to Install Technological Infrastructure × Number of Opioid Prescriptions)

= (215,000,000 ÷ 1,000 × 900) + (67,753 × 900) + (215,000,000 ÷ 1,000 × 1,500) + (5 × 215,000,000)

Calculations suggest the one-time purchase of technological infrastructure over the 10-year period will cost approximately $1.6 billion.

Variable Costs

The following formula was used to calculate variable costs:

Annual Costs of 2D Barcodes Attached to Packages and Labor to Scan

= (Number of 2D Barcodes Required × Price of a 2D Barcode) + (Number of 2D Barcodes Required ÷ Average Number of Barcodes Employees Scan per Hour × Median Wage Rate of a Manufacturing Associate) + (Number of Barcodes Required ÷ Average Number of Barcodes Employees Scan per Hour × Median Wage Rate of a Production Operator Working in Wholesale Distribution) + (Number of Barcodes Required ÷ Average Number of Barcodes Employees Scan per Hour × Median Wage Rate of a Pharmacy Technician)

= (2,150,000 × 0.01) + (2,150,000 ÷ 209 × 21.63) + (2,150,000 ÷ 209 × 16.89) + (2,150,000 ÷ 209 × 13.78)

Calculations suggest the annual purchase of barcode units and additional processing labor will cost approximately $55 million annually, or about $450 million discounted over a 10-year span at a 7 percent rate.

The summation of fixed and variable costs shows the anticipated cost to private stakeholders of investing in 2D barcodes. Over the time horizon presented, the PV of costs associated with this option is approximately $2.1 billion

Option 3: Invest in Radio Frequency Identification (RFID) Technology

Assumption	Value	Justification/Source
Relative Inventory Transparency Associated with RFID Technology	135%	Case Study on Walmart's Transparency when switching to RFID[11]

[11] Ibid

Reduction in Treatment Admissions per 10,000 Individuals Ages 18-24 associated with RFID Tags in Prescription Monitoring	7.8	135% of the baseline barcode effect of 5.8 fewer admissions
Cost of a RFID Tag	$0.01	RFID4U estimate
Number of RFID Tags Required	215,000,000	One for each opioid prescription[12]
Cost of a RFID Handheld Reader	$3,000	RFID4U estimate
Number of RFID Handheld Readers Needed	67,753	One for each pharmacy in the US[13]
Cost of a RFID Fixed Reader	$2,000	RFID4U estimate
Number of RFID Fixed Readers Needed	215,000	Employees should purchase one RFID fixed reader for every 1,000 tags scanned[14]
Cost of an Industrial RFID Printing Encoder	$4,500	RFID4U estimate
Number of Industrial RFID Printing Encoders Needed	215,000	Employees should purchase one RFID fixed reader for every 1,000 tags scanned[15]

[12] CDC, 2017
[13] Qato et al., 2017
[14] Advanced Mobile Group, n.d.
[15] Ibid

Number of RFID Tags Scanned Per Hour	4,767	Study on item-level tagging for retail operations[16]

Effectiveness

The effectiveness of a RFID tracking system was calculated using findings the same study that determined mandatory state-level PMPs are associated with a 5.8 reduction in substance abuse treatment admissions per 10,000 individuals ages 18 to 24 (2017). In addition to projecting effects beyond the 10,000 sample, effectiveness for this option had to consider the comparative advantage of RFID over barcode technology in inventory management. Findings taken from analysis of Wal-Mart, which recently switched to RFID technology, suggests the remote tags improved inventory transparency by approximately 35 percent. This comparative boost when switching to RFID tags was then applied to the study's baseline effect on treatment admissions to differentiate effectiveness between options.

Reduction in Treatment Center Admissions for Individuals Ages 18 to 24 in the US

= Total Number of Individuals Ages 18 to 24 in the US ÷ Population Sample Used in Study × Effect on Population Sample Found in Study × Inventory Transparency Associated with RFID Technology

= 30,850,000 ÷ 10,000 × 5.8 × 1.35

Effectiveness calculations suggest a RFID tag tracking program will result in 24,156 fewer treatment admissions annually, or approximately 241,556 fewer over the 10-year analysis.

Fixed Costs

The following formula was used to calculate fixed costs:

Technological Infrastructure Costs

[16] Advanced Mobile Group, n.d.

= (Number of RFID Fixed Readers Needed × Price of a RFID Fixed Reader) + (Number of Pharmacies in the US × Price of a RFID Handheld Reader) + (Number of RFID Printing Encoders Needed × Price of an Industrial RFID Printing Encoder) + (Labor to Install Technological Infrastructure × Annual Number of Opioid Prescriptions)

= (215,000,000 ÷ 1,000 × 2,000) + (67,753 × 3,000) + (215,000,000 ÷ 1,000 × 4,500) + (5 × 215,000,000)

Calculations suggest the one-time purchase of technological infrastructure over the 10-year period will cost approximately $2.7 billion.

Variable Costs

The following formula was used to calculate variable costs:

Annual Costs of RFID Tags Attached to Packages and Labor to Scan

= (Number of RFID Tags Required × Price of a RFID Tag) + (Number of RFID Tags Required ÷ Average Number of RFID Tags Employees Scan per Hour × Median Wage Rate of a Manufacturing Associate) + (Number of RFID Tags Required ÷ Average Number of RFID Tags Employees Scan per Hour × Median Wage Rate of a Production Operator Working in Wholesale Distribution) + (Number of RFID Tags Required ÷ Average Number of RFID Tags Employees Scan per Hour × Median Wage Rate of a Pharmacy Technician)

= (2,150,000 × 0.50) + (2,150,000 ÷ 4,767 × 21.63) + (2,150,000 ÷ 4,767 × 16.89) + (2,150,000 ÷ 4,767 × 13.78)

Calculations suggest the annual purchase of RFID tags and additional processing labor will cost approximately $110 million annually, or about $770 million discounted over a 10-year span at a 7 percent rate.

The summation of fixed and variable expenses shows the anticipated cost to private stakeholders of investing in RFID technology. Over the time horizon presented, the PV of costs associated with this option is approximately $3.5 billion.

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