Pharmaceutical serialization: compliance and beyond
A holistic analysis
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Executive summary

Regulatory compliance for serialization is increasingly becoming a focus area for pharmaceutical manufacturers and supply chain partners across the world. Most developed and developing economies have either already laid out the regulatory road map for serialization or are in the process of doing so. The regulatory push to secure the pharmaceutical supply chain comes as a result of rising drug-related criminal activities and supply chain inefficiencies. Efforts are aimed at addressing drug counterfeits and unauthorized parallel supply chains, improving supply chain visibility, difficulty in tracking returns or recalls and the paucity of data-driven tools for predicting patient behavior.

The US is leading the way with the Drug Supply Chain Security Act (DSCSA) passed in 2013. The DSCSA road map for end-to-end traceability is stretched across a period of 10 years, with deliverables outlined for all entities of the supply chain. In the US, lot-level traceability began in January 2015 under the act, with package-level serialization to be completed by November 2017. The entire supply chain is expected to be electronically integrated and all nodes of traceability to be established by November 2023.

The European Union (EU) has followed suit with a compliance requirement by enacting the Falsified Medicines Directive (FMD). Unit-level serialization and dispenser authentication have been mandated, with a deadline of February 2019. By 2012, India’s Directorate General of Foreign Trade (DGFT) also mandated serialization of secondary and tertiary levels and set guidelines for the reporting of export shipments. Several other countries have drafted similar regulations for manufacturing and imports.

With India being a major exporter to the US, Europe and other regulated markets, these regulations have a significant impact on Indian pharmaceutical manufacturers.

Implementing serialization across the enterprise requires a holistic approach due to the interdisciplinary nature of the project. The scale of packaging operations, artwork-level changes, integrated information flow, and availability of the right internal and external resources add to the complexity involved.

A detailed project plan and well-defined program management framework is required to enable accountability and timelines. A cross-functional team of packaging, engineering, IT, quality assurance and regulatory affairs is essential for seamless implementation. On the ground, the implementation starts with upgrading the packaging line with additional equipment, modification of the risk evaluation and mitigation strategy, and adaptation to inherent risks.

With significant time and capital, and the thorough planning required for end-to-end implementation of a serialization and traceability program, pharmaceutical manufacturers need to conduct the program judiciously by involving both internal and external stakeholders for its successful execution.
The big picture behind serialization

The life sciences industry and regulators around the world are facing many challenges in protecting the safety of patients. Poor visibility across the supply chain has led to proliferation of drug-related criminal activities such as drug counterfeiting, illegal diversion and theft. It has also caused inefficiencies to surface across supply chain functions. This not only hampers the brand equity of pharmaceutical companies but also puts the life of patients in serious danger. Therefore, serialization laws are fast becoming mandates in many countries.

**Drug-related criminal activities**

Worldwide, there were 3,002 incidents of medicine counterfeiting, illegal diversion and stolen pharmaceuticals reported in 2015, marking an increase of 38% from the 2014 figure. The number of incidents reported in 2015 was the highest in the last five years. This includes a sudden 34% increase in counterfeiting incidents itself, which totaled 971 in 2015.

<table>
<thead>
<tr>
<th>Year</th>
<th>Total Number of Incidents</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>1,986</td>
</tr>
<tr>
<td>2012</td>
<td>2,018</td>
</tr>
<tr>
<td>2013</td>
<td>2,193</td>
</tr>
<tr>
<td>2014</td>
<td>2,177</td>
</tr>
<tr>
<td>2015</td>
<td>3,002</td>
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</tbody>
</table>


A majority of the seizures (56%) reported in 2015 were of non-commercial size (1,000 dosage units or less), while 33% were commercial-sized seizures (more than 1,000 dosage units).

A total of 128 countries across 7 regions in the world experienced a drug-related criminal activity.

**Breakdown of drug-related criminal incidents by region (2015)**

<table>
<thead>
<tr>
<th>Region</th>
<th>Incidents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia</td>
<td>1,100</td>
</tr>
<tr>
<td>North America</td>
<td>779</td>
</tr>
<tr>
<td>Latin America</td>
<td>494</td>
</tr>
<tr>
<td>Europe</td>
<td>358</td>
</tr>
<tr>
<td>Eurasia</td>
<td>265</td>
</tr>
<tr>
<td>Africa</td>
<td>244</td>
</tr>
<tr>
<td>Near East</td>
<td>135</td>
</tr>
</tbody>
</table>


Note: Near East refers to a group of countries located in North Africa and the Arabian Peninsula of Asia including Morocco, Algeria, Tunisia, Libya, Egypt, Lebanon, Israel, Syria, Jordan, Iraq, Kuwait, Saudi Arabia, Yemen, Iran, Bahrain, Qatar, U.A.E. and Oman.
More than one-third of the incidents were recorded in the Asia-Pacific region, where the number crossed the 1,000 mark for the first time in 2015. In North America, the number of incidents more than doubled from 2014. The incidents reported in 2015 involved 1,095 different pharmaceutical products.

Medicines in the genitourinary, anti-infectives and central nervous system (CNS) therapeutic categories reported the largest number of counterfeit incidents, with the highest growth (65%) recorded in the genitourinary therapeutic category.

The international counterfeit drug market generates US$200 billion a year, out of which internet sales account for US$75 billion. An estimated 1% of medicines sold in developed markets are counterfeits, whereas in developing countries, the proportion of counterfeit products out of the total medicines sold is 10% to 30%. In the US, 80% of counterfeit medicine enters the supply chain from other countries.

Counterfeiting happens in a variety of ways. It can range from mislabeling medication with the intent to replicate an authentic approved product to the far more dangerous practices of selling medication without the active ingredient or adding an insufficient or excessive amount of the active ingredient. Counterfeit medicines also sometimes contain extraneous or harmful chemicals.
Inefficiencies in the supply chain

According to Interactive Data Corporation (IDC), the pharmaceutical industry loses on average 4.5% of its potential revenue because of supply chain inefficiencies. Complexity of the supply chain, in which drugs change ownership multiple times before reaching the patient, leads to these inefficiencies. With some channels ignoring distribution rules, a drug’s authenticity is put at stake in the end.

Poor visibility of the supply chain leads to drug shortages, returns and recalls, resulting in higher costs for pharmaceutical companies and health care stakeholders. Premier Healthcare Alliance estimated in 2013 that US hospitals incur drug shortages worth US$416 million annually.

Reimbursement fraud

Another major challenge faced by governments in many countries is fraudulent reimbursement claims. France reported revenue losses between €10 million and €20 million every year from reimbursement fraud. Fraudsters were collecting multiple prescriptions for the same drug, purchased against prescriptions in multiple pharmacies under the social security fund. Later, the drugs were sold in foreign countries at higher prices. Italy faced similar issues, which led to the enactment of the Bollini Law in 2005, one of the first serialization laws to be enacted. Belgium followed suit in 2006 with its EN 011934 law, with the same purpose. In 2010, the Turkish Ministry of Health came up with the serialization mandate to address rampant reimbursement fraud, which was costing the state around US$150 million per year.

Thinking beyond compliance

The benefits of serialization spread far beyond compliance. Unfortunately, entities are so burdened with the stress of compliance that the activity is purely being looked upon as an irrecoverable expense. A farsighted view of the supply chain with well-defined traceability is likely to offer many avenues to gain channel control and plug revenue leakages. For example, product returns and associated credit tracking is a nightmare with complex pricing contracts involving skip-level supply chain partners. Item-level traceability may bring considerable gains in this space.

1 Inventory visibility

Inventory visibility: this enables improved inventory monitoring at various supply chain nodes and assists in forecasting demand more accurately, thereby avoiding revenue loss due to stock-outs.

2 Advanced analytics

Advanced analytics: serialization will be a great enabler for running advanced analytics programs to gather deep insights into consumption patterns, geographical penetration, sales and marketing spend effectiveness, etc. An example would be to map patients geographically using product authentication tools integrated with Global Positioning System (GPS) tracking.

3 Track regimen compliance

Track regimen compliance: usage of weekly dosage packs are on the up. Item-level serialization helps with accurate tracking of the end consumer; for example, sending refill reminders based on the analysis of both prescription data and authentication data.
The global serialization movement

Italy and Turkey took the first steps to enact laws around serialization. Momentum picked up as some US states followed suit. The regulatory landscape became complex in the US, with different versions of serialization mandates. California’s was widely seen as the most difficult of them all.

To take control of the situation and to have one unified law across the US, which is also the biggest pharmaceutical market in the world, the Federal Government passed the DSCSA in 2013 and set a 10-year timeline to implement serialization and traceability down to the item level. By the end of May 2016, most of the developed and developing markets had either concluded serialization regulations or are about to implement them.

Serialization implementation in the US

As the US mandates comprehensive regulations to promote pharmaceutical supply chain improvement, the time to act is now. With most of the Food and Drug Administration (FDA) regulatory milestones and compliance requirement of lot-level traceability already behind us, manufacturers must now undertake the necessary infrastructure changes to comply with the norms. The implementation will require serialized trade item information be encoded in 2D barcodes (GS1 DataMatrix), which can be applied at lot level (bundles, cases and pallets) and at medicinal sales unit or package level. Manufacturers must serialize their products with these 2D barcodes by November 2017, according to the DSCSA.

The 2D barcode typically contains the following elements: Global Trade Item Number (GTIN), expiration date, batch or lot number and serial number.

<table>
<thead>
<tr>
<th>Serialization implementation timelines in the US</th>
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<tbody>
<tr>
<td>November - DSCSA enacted</td>
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<tr>
<td>May - guidance on identifying suspect drug products in the supply chain</td>
</tr>
<tr>
<td>November - Third-Party Logistics (3PL) reporting to FDA begins</td>
</tr>
<tr>
<td>January - wholesale reporting to FDA begins; publicly available database for wholesale distributors established by FDA</td>
</tr>
<tr>
<td>November - licensing standards for 3PLs; licensing standards for wholesalers; guidelines on processes for waivers; exceptions and exemptions; final guidance on grandfathering product</td>
</tr>
<tr>
<td>- packages receive T3</td>
</tr>
<tr>
<td>January - manufacturers send, and wholesalers, distributors and repackagers receive, T3; manufacturers begin lot-level traceability</td>
</tr>
<tr>
<td>November - repackagers serialize product</td>
</tr>
<tr>
<td>November - distributor and wholesaler traceability</td>
</tr>
<tr>
<td>November - pharmacy or dispenser traceability</td>
</tr>
<tr>
<td>November - package-level traceability</td>
</tr>
<tr>
<td>Source: EY analysis.</td>
</tr>
<tr>
<td>Note: T3 - transaction history, transaction information and transaction statement.</td>
</tr>
</tbody>
</table>
Serialization implementation in other key markets

A majority of the key markets around the world have already developed serialization regulations and begun implementing them to secure local drug supply chains. While rolling out the 2D barcodes on the product at the package or lot level through serialization, most of these markets have also developed a mandatory government database for reporting requirements such as China Food and Drug Administration (CFDA) managed database in China, Pharmaceuticals Track and Trace System (iTS) system in Turkey, Administración Nacional de Medicamentos Alimentos y Tecnología Médica (ANMAT) managed system in Argentina, Drugs Authentication and Verification Application (DAVA) portal in India, Korean Pharmaceutical Information Service (KPIS) portal in South Korea and Agência Nacional de Vigilância Sanitária (ANVISA) managed database in Brazil. In the EU, the mandatory uploading of serialized trade items into an institutional hub for verification is already in effect.

To comply with regulations, pharmaceutical companies must maintain their own databases, including their normal regulatory filing information, their schema for handling serial numbers and the exchange of serial number information throughout the supply chain through a track and trace system. These databases have become known as Electronic Product Code Information Services (EPCIS) databases, the software and support services for which are provided via EPCIS providers.
Holistic systems thinking: serialization is beyond packaging lines

Serialization is largely being viewed as a packaging line upgrade project with minor enhancements in IT infrastructure and back-end transaction systems. We agree that the root of the serialization program is at the packaging line level, but successful execution of this program requires a systems thinking approach.

What is systems thinking?

Every system has a series of subsystems, which sum up to the whole. Systems thinking is a method of critical thinking by which you analyze the relationships between subsystems instead of viewing the subsystems in silos. This approach helps in understanding integration complexities, enables better customization for country-specific requirements, facilitates more secure and reliable data exchange among multiple subsystems, and generally allows for more holistic decision-making.

The serialization process is a classic case of a complex system spread across multiple levels – in this case, five levels, as defined by ISA-95, an international standard from the International Society of Automation (ISA). Each subsystem hosts challenges of its own. However, these challenges need to be viewed in consideration of the other enterprise systems that need to be closely connected during the serialization program. This creates an opportunity for review of underlying complexities and functional interconnections that can lead to efficiencies and performance improvements that have widespread benefit and promote multiple business objectives.
Serialization as a subject matter for the pharmaceutical industry has evolved dramatically over the last three to five years. The maturity of various subsystems has also evolved over this period. While subsystems in levels one to three have more or less matured, enterprise- and network-level systems are still in a state of flux. Manufacturers, who form the core of the serialization program, need to implement solutions across all five ISA levels. This is where a systems approach is critical, where the future states of all subsystems have to be considered while drawing a firm-wide strategy.

Source: EY analysis.
India: moving from serialization to traceability

In India, most manufacturers began their serialization programs to satisfy the DGFT requirements for export markets, laid out in early 2011. The DGFT has been following a phased approach where the definition of different phases is laid out a few months before the implementation is mandated. This is the biggest challenge for Indian manufacturers, as the visibility of the road map extends no later than the next pit stop. This forces manufacturers into a piece meal approach, thinking only of the next step.

However, with regulations around the globe taking shape, the trend is now clearly visible. The end objective of all the regulations is traceability, where serialization is acting as the key enabler; however, it is only an enabler. DGFT regulation is also gradually moving toward this. Taking a cue from global proceedings, it will be beneficial for Indian manufacturers also to relook at their serialization programs with traceability as a core component of the strategy.

Most Indian manufacturers have already implemented serialization at the line level in one way or another. However, not much thought has been put into scalability and integration of these components into the larger ecosystem, which includes an enterprise-level strategy and supply chain strategy. This is where a systems thinking approach would help.
A comprehensive approach ensures success

Implementation of serialization has a ripple effect on various business functions within the organization, creating the need for collaboration among different departments. In the production line, the packaging, IT and engineering departments have to work in sync with each other to complete the line remodeling. In addition, an efficient quality review mechanism needs to be set in cooperation with the quality assurance department. Outside the organization, the program needs an effective coordination plan with both upstream and downstream trading partners to enable traceability of the products in the supply chain.

In conclusion, the program needs thorough planning, time, capital investment and, most importantly, attention from the top management. Although IT is a major enabler, to make the process seamless and successful, implementation of serialization requires careful program management that involves multiple internal and external stakeholders.

**Implementation of serialization in phases**

1. **Develop a detailed project plan and overall budget**
2. **Identify all components for serialization journey**
3. **Establish a cross-functional team**
4. **Check compatibility with various trading partners and third parties**
5. **Install sophisticated systems and equipment**
6. **Invest in protocol development and training of staff**

Source: EY analysis.

**Develop a detailed project plan and overall budget**

Serialization projects are complicated and take a long time. Large, multinational pharmaceutical companies easily spend a year pilot testing for a single packaging line. Considering the implementation beyond the pilot for 10, 20, 30 or 60 lines, enterprise-wide, effective and efficient project management comes into play. Therefore, the project management team must execute various project requirements such as resource allocation, define return on investment, manage procurement and contracts, define the scope of the project and schedule events properly throughout the life cycle of the project.
Identify all components for serialization journey

Serialization is not just about changes in packaging line systems or upgrade of ERP for better material management. Organizations need to identify various components such as the readiness of the ERP system as a master data repository, changes in artwork for all affected Stock Keeping Units (SKUs) and new systems such as the enterprise serialization manager, packaging line system and edge systems. You may also need to upgrade your warehouse management software and hardware. Careful planning for the required components will not only save time and money; it is also critical to building an integrated system architecture that supports seamless information flow.

Establish a cross-functional team

This enables necessary communication between different departments in the enterprise. For instance, during serialization implementation, the IT department might come up with an IT strategy in isolation without consulting the packaging and regulatory affairs departments. Meanwhile, the packaging engineering team purchases equipment without discussing it with the IT department. Without a cross-functional team in place and proper communication procedures between them, both the equipment and IT strategy would prove to be useless. The company must also have a robust regulatory affairs team (internal or outsourced) to keep track of the ever-changing regulatory requirements.
**Check compatibility with various trading partners and third parties**

The company must leverage GS1 EPCIS standards to achieve interoperability of data with contracted partners. Trading partners with whom EPCIS event data are exchanged will request supply chain master data about products, company and locations that will be referenced in EPCIS events. The company also needs to gain real-time visibility and enable exchange of serialization information with the chief product or marketing officer.
Install sophisticated systems and equipment

Replacing or retrofitting the existing packaging line must be carried out to implement serialization. The overall cost to upgrade a packaging line for serialization runs into millions of dollars. Typically, various systems, such as package execution system controllers, supervisory control and data acquisition, and programmable logic controllers and devices, are needed to obtain serialization information at different levels (device level, line level, plant level and enterprise level) and then relay it to the stakeholders in the supply chain. Integrating these systems with the enterprise-wide Manufacturing Execution System (MES) and ERP systems for master material data is required to avoid additional line downtime. The company also has to take appropriate measures to maintain the speed of production during a serialization drive, since it is believed to cause an initial loss of 8% to 10% in overall equipment effectiveness. If a line packages products for multiple jurisdictions, it will need to be flexible enough to support multiple serialization and coding requirements. Foolproof systems also need to be installed to check for aggregation, i.e., to check for printing of electronically associated serial numbers on both packages and lots to confirm that a particular package is meant for the intended lot.

Invest in protocol development and training of staff

As the packaging line equipment gets upgraded to drive serialization, making relevant changes to standard operating procedures and work flows involved in that line’s operation also become necessary. It is also important to update the company’s risk evaluation and mitigation strategy accordingly. In addition, training of technicians and operators on the upgraded equipment becomes critical to success of the serialization project.
Instead of taking it as one more compliance activity, organizations should view their serialization program as an opportunity to review and renew business processes, data flow and applications from production to supply chain. A major transformation program such as serialization requires integrated efforts from major business functions. If planned properly, it will help the business to streamline underlying processes, assist in future-ready investments and establish a single version of truth.
References


“Leveraging track and trace in the pharmaceutical industry,” Frequentz, 2014, p. 2.


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As populations age and chronic diseases become commonplace, health care will take an ever larger share of GDP. Scientific progress, augmented intelligence and a more empowered patient are driving changes in the delivery of health care to a personalized experience that demands health outcomes as the core metric. This is causing a power shift among traditional stakeholder groups, with new entrants (often not driven by profit) disrupting incumbents. Innovation, productivity and access to patients remain the industry’s biggest challenges. These trends challenge the capital strategy of every link in the life sciences value chain, from R&D and product supply to product launch and patient-centric operating models.

Our Global Life Sciences Sector brings together a worldwide network of 15,000 sector-focused professionals to anticipate trends, identify their implications and help our clients create competitive advantage. We can help you navigate your way forward and achieve sustainable success in the new health-outcomes-driven ecosystem.

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