“Bridging the Value Chain” – The Pedigree Way

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Abstract

1 Serialization – Need of the Hour

Lack of global co-operation on agreement with one common technology over the years has delayed the process of serializing the drugs. By and large, majority of the regions have come up with consensus to have a Unique level Identification Code (UIC) on unit level pharmaceutical products. With almost 40% of drugs being fake in the developing markets like Turkey, China and Argentina; these countries have been the prime movers in serializing drugs. However every region has its own technology and deadlines to meet the same. For e.g. China, one among the early movers implemented linear code serialization instead of 2D-style packaging. Other markets will be following the suite in coming years and that includes South Korea, Brazil, the U.S, and the EU. The requirements and guidelines for serialization are country specific, which is why pharmaceutical companies operating internationally need flexible solutions to meet the regulation.

2 Synopsis

Counterfeiting is a multi-billion dollar issue and is a threat to the pharma industry. Counterfeiters have started using advanced technology to manufacture and label products, sometimes even better than the original products. Off the total counterfeit market, less than 5% contribute to the developed drug market and 40% from the emerging markets. On account of this, though not a complete solution but to ensure patient safety, to track the value chain of drugs and to protect the brand of pharma companies, Serialization was introduced in the year 2011. In 2013, the US and Europe mandated this as a law and intimated manufacturers to serialize their drugs and aggregate the supply chain manufactured by 2023. Since the whole process would take some time to fall into place, in the initial phase (by mid-2015) drugs are to be labelled with unique "Product Identifier" code followed by aggregation of the whole value chain in other words the pedigree way. This whitepaper would discuss on how the contract manufacturers and pharma companies have acted on this regulation with case studies. The paper would also focus on cost involved in implementation and maintenance of serialization in the product lines and how top CMOs like Vetter, Recipharm etc. have achieved success with serialization in respective regions

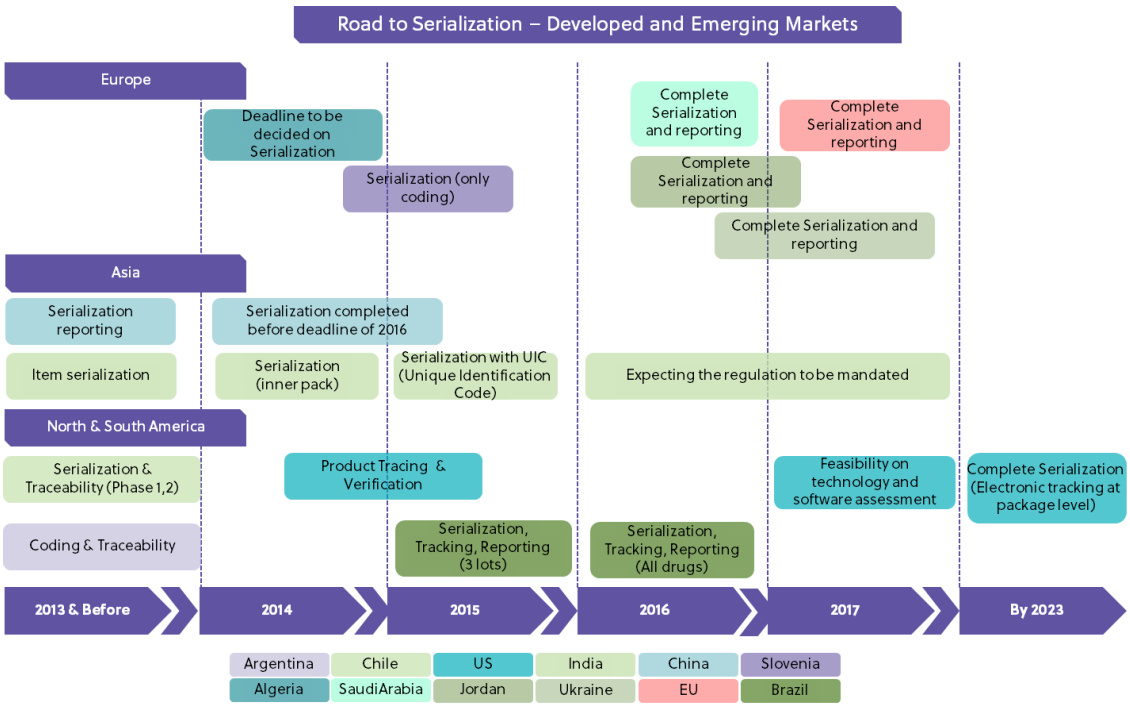
3 Recommendation

Upgrading production and packaging lines with serialization process would aid pharmaceutical companies and CMOs in achieving a better visibility in the drug value chain and in maintaining the brand image of companies by eradicating fake drugs in the market thus providing patients with safe drugs.

"2013 to 2023" – Serialization a Decree!

Serialization requirements are in various stages of development in the EU and in its member nations, as well as in Turkey, India, China, Brazil, Argentina, and Korea. The new federal mandate extends the deadline to 2023, but requires product identifiers (includes therapeutic category, dosage and route of administration) to be added to each package and homogeneous case of product by November 2017.

Europe's new Falsified Medicines Directive, requires authenticity features on prescription drug packaging, allowing verification of individual packs throughout the supply chain, and overall security issues within the distribution network. The European directive also demands strengthened requirements for control and inspection of active substances, regardless of where ingredients are manufactured.



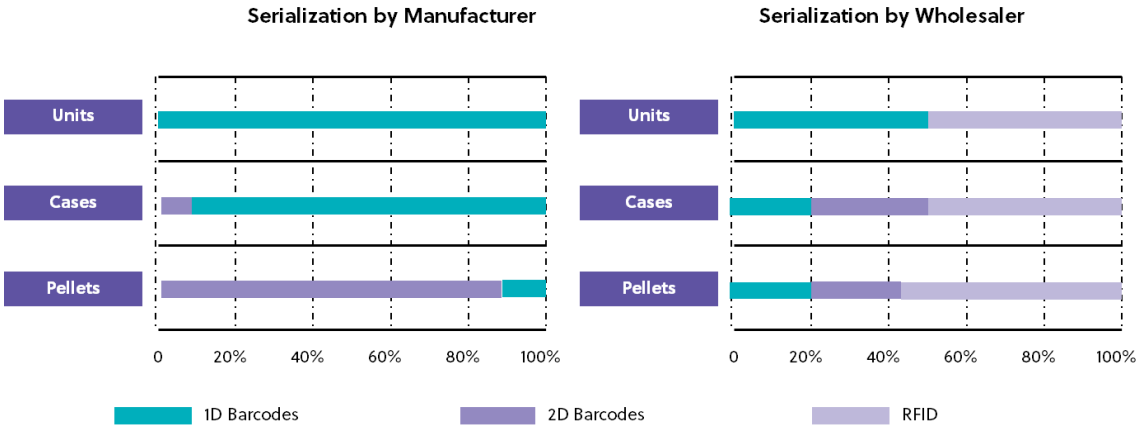
Source: Government databases of US, EU, India, China, Algeria, Saudi Arabia, Ukraine, Brazil, Argentina

California announced the E-Pedigree law in 2014. As per the law all pharmaceutical manufacturers and distributors are mandated to implement serialization in production and packaging. By 2015, manufacturers are obliged to incorporate product transaction data into a single document that is available, either electronically or on paper, each time ownership is transferred. This is to be performed for 50% of the products by 2015 and the complete process of drugs by 2016. The document must include transaction data listing lot level information, a complete transaction history, and a transaction statement and must be maintained for six years after the transaction. By November 2017, that information must be available electronically, and the product identifier must be affixed or imprinted on the label at the product and case level. All drugs should be serialized completely by 2023 and the customers should be able to track the same at ease.

Understanding the Methodology of Serialization

Serialization on drug packaging can be -done through three different technologies: One dimensional (1D) barcodes, Two-dimensional bar codes (2D) and Radio Frequency Identification (RFID). Different countries across the globe follow any of these methodologies depending on the regional law. These technologies track a drug from the smallest scalable units to pallets. Universally pharmaceutical manufacturers/CMOs have preferred 10% use of 1D & 90% 2D in cases and 85-90% use of 1D in pallets & remaining in 2D. Having said all this 2D bar code type technology is considered to be a cheap and effective technology.

Illustrated below are the results of a survey conducted among pharmaceutical manufacturers and wholesalers and their preference to using technologies. The manufacturers and wholesalers included in the survey are those who handle huge volume of drugs at their sites.



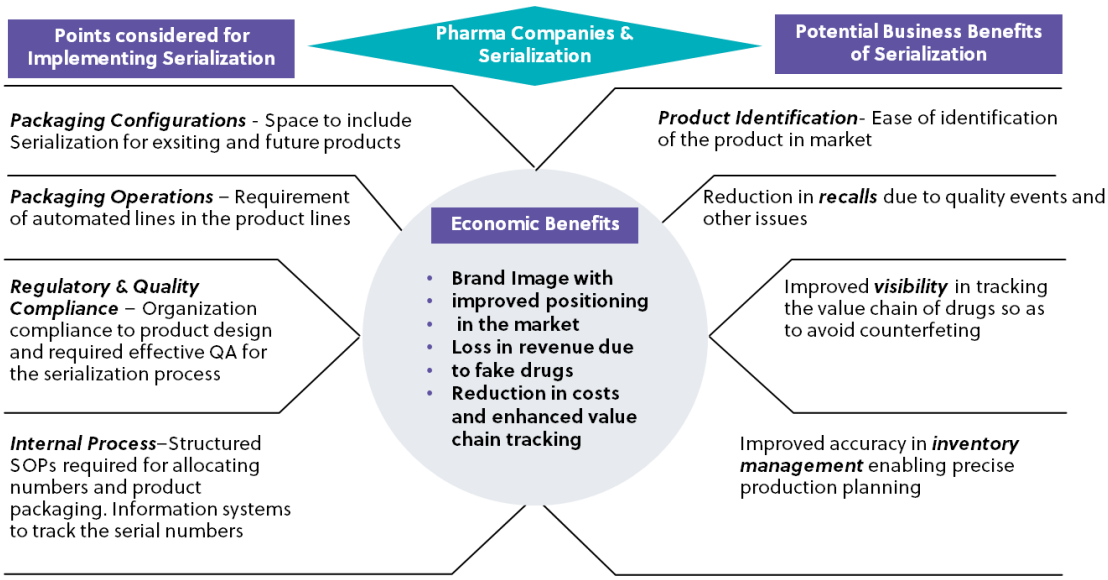
Source: Survey by Contract Pharma

Pain Points in Implementing Serialization

Number of challenges are required to be addressed while implementing Serialization. Overall Equipment Effectiveness (OEE) is something which cannot be ignored during the implementation of serialization. Some of the challenges that might impact the OEE are elucidated below

- Mismatch of equipment used in the production lines might lead to hassle in the lines
- Adding inspection and tracking equipment adds to cost and drop the line speed leading to lower productivity
- New equipment addition occupies extra space in the lines
- Vibration in the lines caused during production might lead to problems during inspection
- Volume of data to be recorded (internal plant line level or plants integration globally) will be high in future and the storage capacity has to be intact and flawless to record all the information

Potential Benefits of Serialization



Source: Beroe Analysis in collaboration with Experts

"Jump on the Bandwagon" – CMOs & Serialization

Many small and medium CMOs in the industry have been slow in implementing serialization in the past years due to cost of deployment, lack of regulations and customer commitment. Some of the major reasons why CMOs were reluctant to deploy Serialization at their plants:

- Different sized batches
- Frequent Label Format changeovers affects productivity and costs
- Multiple Customers

However with laws making serialization mandatory, major CMOs have started moving more proactively with serialization readiness strategies and are keen to grab business opportunities coming in the future. Explained below are major CMOs and their successful implementation in emerging markets

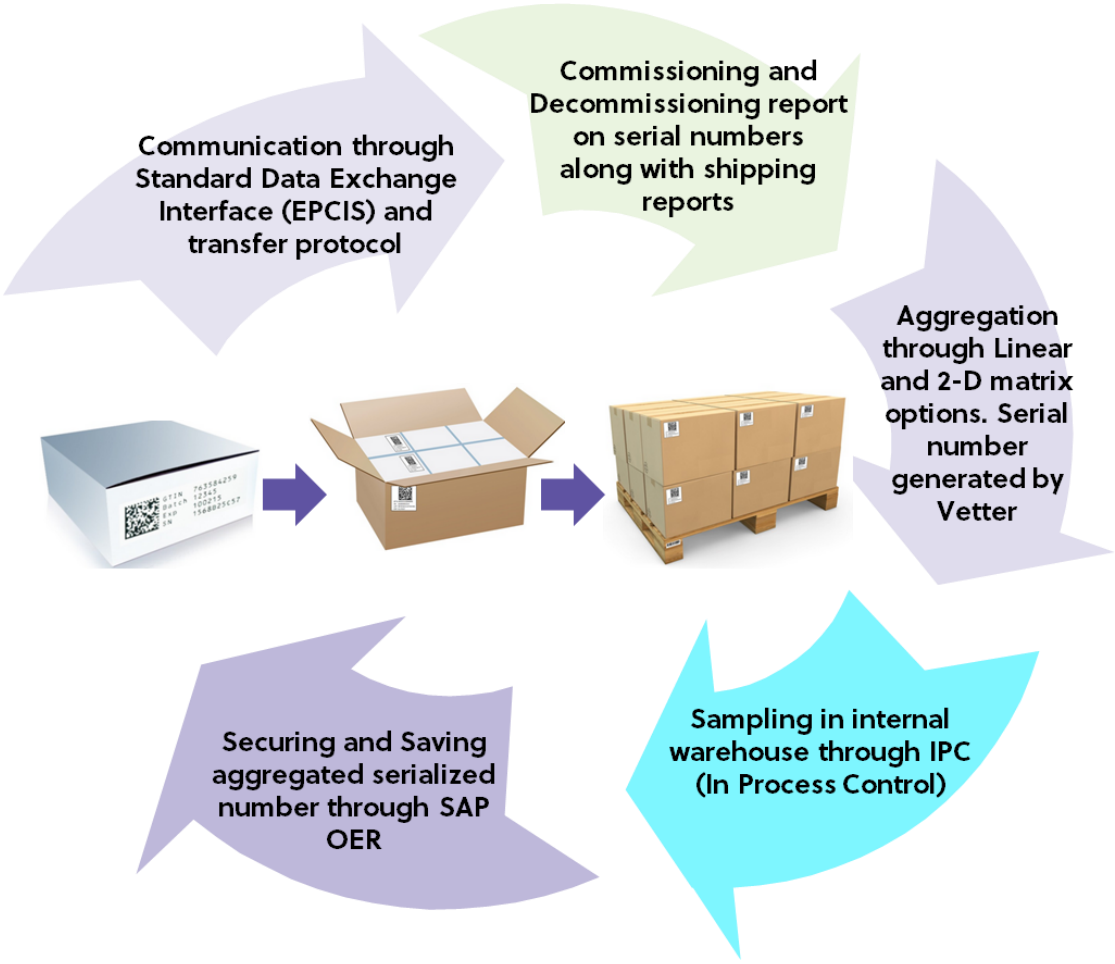
How have the major CMOs/CDMOs succeeded in serializing drugs?

Aesica, whose key market is *China,* has successfully met the new serialization requirements in China in just 3 months. China being a highly regulated industry and to prevent drug counterfeiting & recall, Aesica was forced to implement serialization in their lines. Now the company can track each individual packaging unit down to the smallest sellable unit which is the e-pedigree model. Aesica is in the process of implementing the same to all its sites world-wide

- Implementation technology: Thermal ink-jet technology to print stickers and 2D barcodes
- Duration: 3 months in collaboration with QAD

Recipharm serialized 57 batches of drugs supplied to *China* in Feb. 2014 in six months using an adaptable and methodological approach. The company used 1D barcode technology and unique serial number. Recipharm completed serialization in March 2015 project for *Abbott* for the *Korean* market. This project was said to have started in 2014.

Vetter Pharma came up with a flexible solution which can be implemented in any region and by multiple customers. The system uses EPCIS (Electronic Product Code Information Services) and 2D matrix with aggregation of all the production and packaging lines.



Exemplified below is a brief on Vetter's serialization solution

Following are the major benefits accomplished by CMOs after implementing Serialization

- Each individual packaging unit can be identified to the smallest sellable unit.
- Aggregate individual unit serial numbers are bundled, boxed and placed on shipping pallets as packages
- Flawless track and trace of every single pack of medication.
- Serial numbers are reported to the required government agencies once the products are produced and imported.

With outsourcing growing at 10 to 15% and pharma companies shifting to end-to end service with CMOs, they have started to rely more on CMOs. This has increased the pressure on CMOs to deliver quality products with better visibility of the supply chain. Thus implementation of serialization in the production lines of CMOs would be a key to success to their future

Road ahead for Pharma Companies

In the past 2 years pharma companies have focused on emerging markets like China, Turkey, Brazil, Argentina etc. implementing serialization at their plants. However with the Californian and EU laws enforcing serialization as a mandate, the companies are striving to achieve the same in the coming years. Pharma majors like Pfizer, Merck, Daichhi Sankyo, Sanofi have partnered with solution providers to make their production and packaging lines serialized

Approaches to Serialization

There are two approaches to implement serialization in a pharma plant. They are top down and bottom up approach which are briefed below

Bottom up: This is the most common approach where there are vendors in the market who would provide *Mark and Verify* Modules. The module integrates a marking device, camera and an eject station. This is also combined with Tamper Evident Labelling machines for a secure printing process. The lines have in-built databases to store information. Integrating this system to ERP and software platforms is the next step for the value chain serialization (in other words pedigree)

Top down: In this approach, the consideration is that cameras and line marking devices are available. Now the User Requirement Specifications (URS) which is a tedious process is to be integrated with independent lines in plants and sites and also connected through ERP with all the sites simultaneously.

This is done through interface platforms connecting ERP and MES (Manufacturing Execution Systems). There is another platform where the data in each line is not stored in the lines due to confidentiality whereas it is stored in common servers inside the plants

At least 60% of the drug manufacturers are in the process of implementing serialization With 80% of the manufacturers equipped with ERP system, they are in the process of following top down approach

Overall companies/CMOs (e.g. Pfizer, UCB etc.) with established lines follow top down approach and they have been successful

Generally, big pharma companies perform serialization in-house for their products manufactured at their facility with IT solutions. For outsourced drugs to CMOs, big pharma companies partner with these CMOs under mutual consent and implement serialization in the production lines

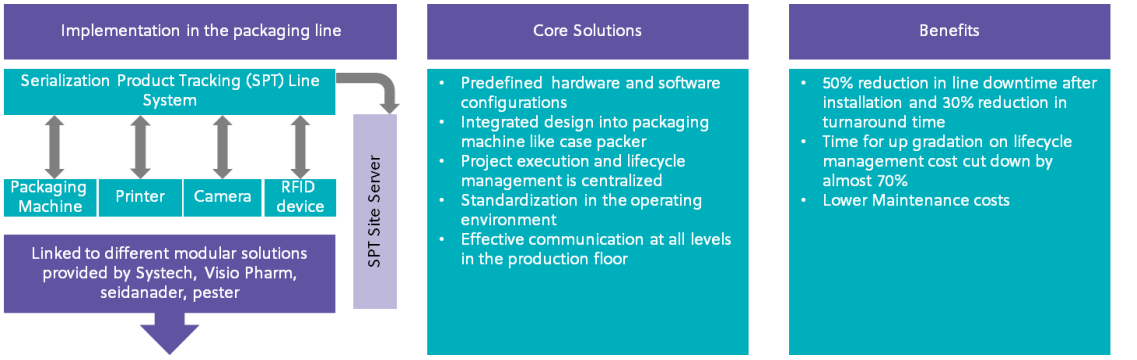
Who to engage with?

Illustrated below are the partnerships were pharma companies and CMOs have engaged with solution providers for serialization

- UCB with Advanco & Kezzler – Serialization Partnership to protect drugs in the domestic market of India and this is to be rolled out by mid-2015. This technology (Unique Identification Code) allows consumers to directly SMS the code to get the information on genuine medicine and that the drug is not subjected to recall.
- Aesica partnered with QAD
- AstraZeneca with Axway & Systech– Axway: Serial numbers fed to 33 production lines at 10 sites in 2011. Systech: To provide packaging line serialization systems to all the plants globally
- Merck with Nasco – Nasco is experienced in 2D matrix and RFID

Novartis – A case

The illustration below depicts how Novartis integrated technical platform and IT infrastructure into their packaging lines and achieved measurable qualitative and quantitative benefits through serialization



Source: Novartis

Cost of Implementation and Maintenance – Serialization

With Avastin, Roches' drug found to be counterfeited, the US government mandated laws on packaging and to implement 2D matrix codes. In-spite of the US being a well regulated market and fake drugs contributing to less than 5% of drugs in the region, customer safety has always been of foremost importance. This has led to the Californian government passing the e-pedigree law. At least 60% of the drug manufacturers are in the process of implementing serialization in their manufacturing plants.

With 80% of the manufacturers equipped with ERP system, they are in the process of following top down approach/model as spoken above. Given the situation let us understand what would be cost incurred to implement serialization in the production and packaging lines from manufacturer's perspective. The illustration below shows the installation cost of serialization as estimated by the manufacturer. Costs which involve maintenance and data sharing with ERP and other modules are an approximate figure provided by the vendors who provide the service. These vendors are large enterprises who provide management software solutions and have included all the costs associated with the implementation and running of serialization.

The approximate costs are with respect to a medium level company. As illustrated, the variation in the range of cost is more because the actual cost of implementation and running serialization solely depends on the business model followed by the company and use of equipment. For e.g. in a high speed production line, the equipment used for serialization also has to be a high speed automated equipment so that the efficiency in the process is not compromised.

2D Matrix and RFID both offer better visibility in the pharma value chain, however the cost of implementing and maintenance depends on the automation technologies

The costs illustrated below are also in line with costs estimated by Generic Pharmaceutical Association

Estimates provided by Manufacturers Implementation Costs				Estimates provided by Vendors Data Sharing and Maintenance Costs		
	Average cost per line	Average cost per site	Average enterprise cost	Implementation Costs		Annual Ongoing Costs
Cost Incurred for Serialization	USD 1.4 million (ranges between USD 400,000 to USD 2.8 million)	USD 980,000 (ranges between USD 120,000 to USD 3.5 million)	USD 12 million (ranges between USD 2.4 million to USD 25 million)	Cloud based	USD 25,000	USD 300,000
				Others	USD 248,000	USD 43,000

Source: Estimates from IT solution provider solutions company

A Safer Drug Value Chain for the Future

Pharma majors like Pfizer, Bayer, Merck, Eli Lilly etc. are in the process of implementing Serialization. In 2014, Eli Lilly has invested USD 110 million in serialization globally by installing computer controlled high speed stamping equipment in 40 packaging lines. Following would be the significant benefits for a pharma manufacturer/CMO who implement serialization in their plants

- Enhancement in supply chain visibility by 60 to 65%
- Reduction in costs and improve efficiencies with respect to recalls by 30 to 35%
- Increase in inventory management by 15 to 20%
- Improvement in procurement automation by 15 to 20%

The above estimated cost through study & expert analysis and analyzing the importance of serialization would aid in a high level investment plan for pharmaceutical manufacturers in the US and Europe as they are mandated to follow the serialization suit in near future.

With e-pedigree tracking, drug recall process can be managed more effectively by knowing the location of products

Be it 1D, 2D or RFID; these technologies are expected to revamp the way drugs are manufactured, packaged and shipped globally. Hope serialization revolutionizes the pharma industry and paves way to a complete anti-counterfeit value chain and most importantly provide safe drugs to customers.

Industry Speak/Acknowledgement

	**Owner of a pharma company** Technological Innovations and trends in Serialization in India
	**Plant Head of a pharma company** Value achieved in serialization the production and packaging units in plants. Cost of implementing and running the serialized drugs
	**Production Manager in a pharma company** Improving the operational efficiency would be the key to improving manufacturing process in India and to compete with developed markets

Metadata

Industry to be impacted (*Highlight the industry to be impacted*)

Pharmaceutical	Food, Beverage & Tobacco	Metal, Mining & Minerals	Chemicals
Oil & Gas	Personal Products	Bank & Financial Services	Hi-tech

Domain to be impacted

CMO Formulations

Category to be impacted

Sterile & Non-Sterile

Focus Area (*Highlight the Focus Area***)**

Technology	Supplier Intelligence	Sourcing Opportunity	Substitute Opportunity
Supply chain Risk	Input Cost	Price Outlook	Sustainability

Keywords Used

Serialization, Regulation, Pedigree

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