



# Product Serialisation to Advance Pharmaceutical Authentication and Patient Safety

## *The Pharmaceutical Industry Takes On a New Global Challenge*

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*The pharmaceutical industry faces complex issues in ensuring patient safety. It must test and provide safety and efficacy profiles on its prescription drugs during clinical trials and throughout the product lifecycle. It must adhere to strict quality control procedures in manufacturing to meet safety guidelines, and then maintain the safety of the product throughout distribution. To do all of this effectively, the industry is facing a new regulatory challenge – that of product serialisation. How the industry meets this challenge will be the defining factor for years to come in how it secures the safety of the patient and supply chain.*

### THE DRIVE TO SERIALISATION

In today's global pharmaceutical distribution environment, the risks to undermine product safety are significant. Counterfeiting and product diversion are major problems and growing. In 2007 the World Health Organization estimated that drug counterfeiting accounted for 1% of sales in developed countries and rose to more than 10% in developing countries.<sup>1</sup> Just a few short years later in 2011, estimates suggested counterfeit drugs can range between 1% to 70% of the total market in developing countries and that even in highly controlled

supply chains, 1% of drugs are counterfeit – and these statistics do not take into account those drugs diverted to street sales.<sup>2</sup> The risks to which patients are exposed in taking these counterfeit products are significant, and the situation is further exacerbated by the increasing overall healthcare costs in markets where counterfeits are distributed. In addition, the pharmaceutical company suffers from lost revenue and potential damage to its reputation as a result of counterfeit products introduced to the supply chain.

So serious are these issues that several countries (the United States, the European Union, China, South Korea, India, Argentina) have already enacted legislation requiring that each prescription unit-of-sale product carry a unique data matrix bar code, and in many instances associated human-readable information, to identify the product (track and trace) throughout its distribution. Many more countries have such regulations being readied. As a result of these regulatory efforts, countries hope to:

- decrease the impact of counterfeit and diverted product,
- improve supply chain visibility/management,
- reduce inaccurate event reporting and strengthening pharmacovigilance efforts,
- and increase patient safety and engagement.

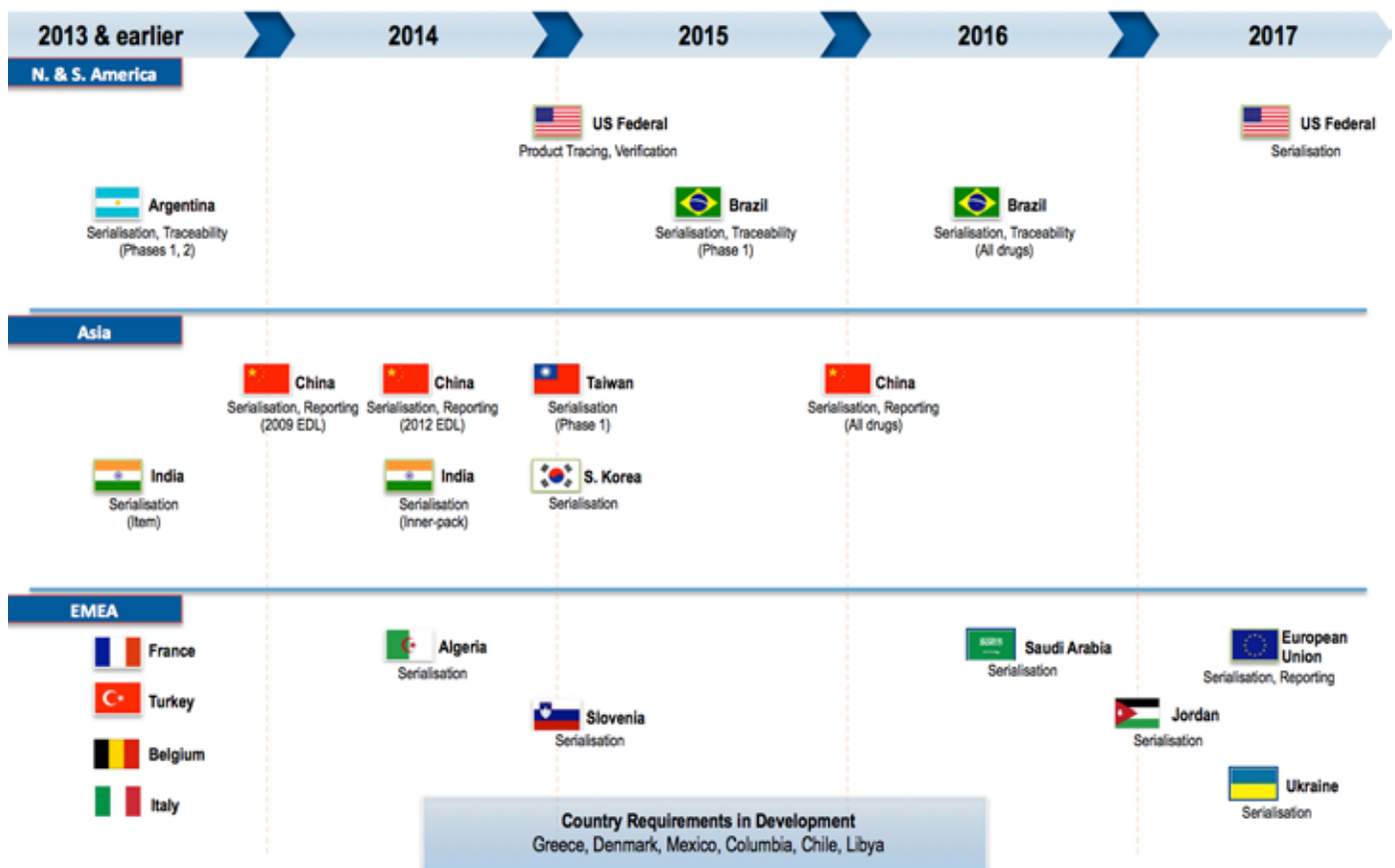


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The two main regulatory movements driving this serialization effort globally are the United States Drug Quality and Security Act (US DQSA), H.R. 3204 enacted as law in November 2013, and the European Union Falsified Medicines Directive (EU FMD). Both of these regulations will be in full effect shortly – the US DQSA in late Fall 2017 and the EU FMD expected in first calendar quarter 2018. However, other countries, such as China, India, South Korea and Saudi Arabia have already enacted regulations requiring serialisation, thereby pushing European and US based pharmaceutical manufacturers into developing serialisation programs for shipments into these countries.

### Global Track and Trace Regulations

*40+ Countries, 75+% of Global Pharma Market Serialized by 2017*



Graphic courtesy of TraceLink



### PUTTING SERIALISATION TO WORK

Serialisation is not new. There have been systems in place for the better part of a decade; one was created initially to distinguish a product in order to meet its REMS requirements. The product was a controlled substance packaged in a blister pack. The manufacturer believed by having a unique product identifier associated with each product in the blister-pack the risk of diversion/counterfeiting would be mitigated. Track and trace capability became a bonus. Some large pharmaceutical companies have developed serialisation capabilities in-house. Other companies rely on their contract manufacturer (CMO) and/or contract packaging (CPO) partners. However, with major market regulations now driving the effort, more companies are now looking for ways to enact this product identification method throughout their portfolio.

Product serialisation involves the printing of a unique data carrier on the product and/or its unit of sale as it is prepared for shipment. At the present time, systems exist to serialise packets, bottles, vials, pouches, cartons, shipper cases, and pallets. Serialisation has also been used for products packaged in blisters, with each cavity bearing its own identifier as well as dissolvable film strips then packaged in pouches. Individual tablets and capsules are currently not carrying unique identifiers.

Most serialisation is done via direct printing on the product or package, although there is some done via labelling (slap and ship), and others utilise bright stocking, which is printing the serialisation information and other market specific information on a pre-printed label with a blank area available for the data code. Presently China requires 1D serialisation, which is a one dimensional bar code type identifier, where only the width of the bar can be altered. Europe and the United States require 2D labelling, which is a presentation of rectangles and squares where both height and width dimensions can be altered. There is also RFID product labelling, which is a radio frequency identifier with its own built-in transmitter.

To start the process, one needs to create a bank of serial numbers to be tied to specific product NDC or registration numbers. To this end, many pharmaceutical companies utilise in-house ERP systems to generate their numbers meeting healthcare guidelines established by GS1. Others might contract with a broker of serial numbers. As with any form of data exchange, complexity sets in immediately. The technology generating the numbers must be able to drive the printer outputting them. The data file (of commissioned serial numbers) must then be captured and transmitted throughout the supply chain so there is an ability to track and trace each product through the supply chain.

Essentially there are four distinct levels of technology required to deliver a comprehensive serialisation and track and trace solution for the pharmaceutical industry:

- **Level 1: The Device Level** – includes line level systems such as printers, scanners, cameras, controls, check-weighers, etc.
- **Level 2: Line Level Control** – includes software that will control the data, the serial number management, and aggregation of data across all of the Layer 1 devices on a specific packaging line. There is one Level 2 system required for each packaging line.
- **Level 3: Site Level Software & Hardware** – includes the software systems to send and receive information to multiple Level 2 systems within each site, and to connect to the Level 4 software, which is typically hosted outside of the company firewall, or in the cloud. There is typically one Level 3 system for each packaging facility.
- **Level 4: This is typically referred to as an Electronic Product Code Information Service (EPCIS).** Level 4 is the software that manages connectivity to the pharmaceutical company as well as connecting all of the Level 3 site level systems across all sites. Level 4 systems will normally be interfaced with ERP systems along with other track and trace related systems in order to provide comprehensive use of serialized and operational data. In some instances, these higher-level systems would constitute a higher architectural layer referred to as Level 5, where the ERP system is considered Level 4.



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There are numerous software and hardware companies working within the industry to support the requirements of these four levels. Many companies have set up lines utilising different providers in order to determine where the best option for service and reliability will reside and to mitigate risk in dealing with only one technology partner. As a result, there is no one solution to establishing a serialisation process although a few key players have emerged within the industry, some offering capability within all four layers, others targeting specific layers.

Once these technology levels are established and the product is labelled and shipped, pharmaceutical companies need to be able to access, process and analyse the data. 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.

### SOME INHERENT CHALLENGES TO ENACTING SERIALISATION SYSTEMS

As one would anticipate, the complexities of serialisation abound when multiple technology systems must communicate with one another to produce and exchange data. Decisions need to be made on the IT infrastructure – what hardware is appropriate, how should the system be wired, what type of maintenance agreements are necessary for upgrades. Should you pursue cloud-based EPCIS solutions and what about vmWare or discrete servers at the packaging facility? Your control systems and Electrical Engineers now need to not only orchestrate the printing and verification of data codes they must also support data collection. How do they want to field map their data; how should they configure their XML files? Although there is a certain baseline of code that can be established, once you reach the detail of the actual product the remaining code is customized. Do you want to set up an inline system or look for a more flexible solution? All computer systems need to be validated and support multifunctional communication,

both internally and with any technology vendors. Then there are legal contracts to consider for licensing cloud-based software and support.

In addition, you need to consider the actual physical attributes of the data mark. Questions such as –Where should the code be positioned on the product/package? What font should be used at what size? How much of the code is human readable and where is it positioned relative to the bar code? What is the readability (ANSI grading) of the data matrix barcode? – These are all points that need to be addressed and then coordinated with any packaging artwork.

These complexities translate to significant costs where a typical line implementation may require between €200k - €500k for start up along with a dedicated team to oversee the operation as well as train operators. Yet serialisation is not just about the technology. Indeed serialisation systems are not yet fully automated, leaving the human factor to be considered. Packaging operators and shipping personnel must be trained to understand the systems and how a smudge or an incomplete character in a printed code, or a rip in a carton or pallet label can eliminate that product or shipment from distribution. Quality control is extended beyond the product itself to also include the readability of the data code, adding another level of accountability to the packaging and shipping operation.

### OUTSOURCING OPTIONS FOR SERIALISATION

Current requirements for serialisation are limited to marking the unit of sale with a unique data carrier. In 2023, the process will be required to support a parent-child relationship, where the product is traceable throughout its journey – from the individual package through the carton/pallet to its final point of distribution. This level of serialisation is known as aggregation and the Healthcare Distribution Management Association (HDMA) in the United States, representing the nation's largest drug distributors, is already suggesting pharmaceutical companies support this aggregation effort. The pressure from groups like the HDMA is pushing pharmaceutical companies to seek solutions to serialisation that can get them up and running quickly.



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Working with contract packaging companies (CPOs) with existing serialisation capabilities is an option that pharmaceutical companies can pursue with little risk to their operation and with limited capital investment. These CPOs have established serialisation processes and offer experienced and trained personnel at all levels to ensure optimum outcomes.

The advantages to outsourcing serialisation to an experienced CPO are many and include:

- Years of experience in serialising a variety of product forms, giving them the process knowledge and accountability checklists needed to accommodate your product quickly. Often as pioneers in the process of serialisation, the established CPOs have learned to improve serialisation processes or avoid costly mistakes.
- Dedicated teams for computer systems management to support serialisation with a thorough knowledge of the protocols required to maintain data communication throughout the chain.
- Trained and highly skilled line operators and shipping personnel.
- Established working relationships with the largest technology and EPCIS companies.
- Established packaging lines for serialisation, some offering flexible serialisation stations through end of line modules that can be moved to other lines as needed.
- Preserving the capital investments needed to support such efforts in-house.

By outsourcing product serialisation to an established CPO, whether as part of a packaging operation or as a standalone service for product already packaged in-house, a life science company can concentrate on the data analysis such serialisation offers to avoid adverse events and optimise channel distribution. Even companies that prefer to keep all packaging and serialisation of their mega brands in-house, may find outsourcing lesser brands a fast and cost-effective alternative to establishing additional serialisation lines to

### LEARNED EXPERIENCE

A case of learned experience is that which established the need to send the list of serial numbers included in a shipment after the physical goods have left the facility. Because goods shipped need to be matched to their list of serial codes upon receipt, it is necessary to send the list of numbers with the shipment. However, once the list is sent there can be no changes. So if a case is damaged at the shipping dock and needs to be replaced, that pallet no longer reflects the original serialised contents of the shipment and will be rejected upon receipt for not matching.

accommodate them, particularly when working with a CPO that utilises the same technology partners. In addition, those companies currently outsourcing manufacturing and/or packaging may look to send their packaged product to a CPO with existing serialisation capabilities to tap into their existing capabilities rather than face the delays and costs incumbent in a serialisation start-up.

### BEYOND PRODUCT IDENTIFICATION – ADDITIONAL BENEFITS TO SERIALISATION

The impact serialisation has on patient safety and supply chain security is a given. However, the use of serialisation in the future will extend these benefits to many other product areas including clinical trial packaging and distribution, specialty biologics and orphan drugs, as well as OTC and nutraceutical products. In addition, pharmaceutical companies can use serialisation to more effectively facilitate product recalls, returns and charge-backs. Indeed, current reliance on lot numbers versus unique individual product identifiers leads to far greater recalls than may be necessary. An example would be a single case or pallet having a cold chain excursion, where only its product, not the entire lot, was impacted.



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Patient interaction is also enhanced when the patient can refer to their unique data marker in conversations with the manufacturer, pharmacist or physician. By using the data tied to that marker, the manufacturer is in a position to provide more timely and accurate responses to patient concerns or complaints thereby increasing compliance and managing to control overall health costs. Manufacturers can also use the bar code to proactively disseminate information and adherence guidelines and programs specific to that patient and his or her condition via websites and smartphone Applications. They can also offer coupons or other reimbursement assistance.

Although the pharmaceutical industry is being mandated to embrace serialisation, those who do so quickly will be in a position to reap the many benefits the program has in store.

### NOTES

- 1 World Health Organization. <http://www.who.int/mediacentre/news/releases/2007/pr07/en/>. Accessed September 24, 2013.
- 2 Pitts P. Counterfeit drugs and China new. <http://www.cmpi.org/inthe news/testimony/counterfeit-drugs-and-china-new>.

### ABOUT THE AUTHOR

Gaurav Banerjee is the Director of Technical Services for US and EU at Sharp Packaging Solutions, a division of UDG Healthcare, Plc. In this role, Gaurav is responsible for the development, documentation, implementation, and enhancement of the UDG Healthcare Packaging Division's serialisation services platform. Gaurav manages technical staff, including project managers and serialisation engineers, who execute technology projects that support customer, supplier or internal service initiatives. Gaurav also oversees and maintains primary business relationship responsibility for vendors and business partners supplying Sharp with serialization services. Prior to joining Sharp in 2012, Gaurav worked in various roles in Operations Management and Regulatory Compliance at Merck & Co, Inc. Before Merck, Gaurav held the positions of Manufacturing Engineer and Supplier Quality Engineer at Metrologic Instruments – which is now a subsidiary of Honeywell. Gaurav holds a Bachelor of Science degree in Commerce & Engineering from Drexel University and a Master of Business Administration from the Pennsylvania State University.

### ABOUT SHARP PACKAGING SOLUTIONS

As a contract packaging company, Sharp Packaging Solutions has been engaged in the serialisation of individual unit dose pharmaceutical products for nearly 8 years. As such Sharp has serialised almost 2 billion unit doses of pharmaceutical products into the US supply chain. As a pioneer in the implementation of serialisation technology in the U.S., Sharp has established relationships with the leading technology providers in serialisation and is now leveraging its expertise in its EU facilities.

Sharp Packaging Solutions is a UDG Healthcare company. UDG Healthcare plc is a leading international provider of services to healthcare manufacturers and pharmaceutical retailers, with operations in 20 countries including the US, Canada, the UK and countries throughout Europe as well as Japan and Brazil. It has approximately 8,500 employees across its global footprint and revenues in excess of €2billion annually.