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The Hidden Challenges of Pharmaceutical Serialisation by Domino Printing Sciences

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Implementing item-level serialisation: technical challenges, commercial benefits

In the almost 40 years since counterfeiting of pharmaceutical products was recognised as a problem by the World Health Organization (WHO), the industry has waged a constant battle against increasingly sophisticated and organised counterfeiters, with drug packaging serving as one of its foremost defences. The true extent of the counterfeiting is unknown, since no global study has ever been carried out, but according to WHO estimates, up to 15% of all medicines are counterfeit and there was a recorded rise of 92% in seizures of falsified medicines between 2005-2011. The problem varies in severity around the world. In some areas of Africa and the Far East, up to 30% of all medicines sold are counterfeit, while estimates of around 1% are the norm in EU Member States. However, the huge growth in sales of drugs over the internet means that national and trading area borders are increasingly irrelevant. This is a global problem and legislatures around the world are taking action to protect patients.

In Asia, Europe, South America and the USA, governments are drafting legislation that will make life that bit harder for the counterfeiters. While each of these schemes has its own particular characteristics, a fundamental premise of each is item-level serialisation, that is, assigning a unique identity to each unit of sale, typically a single pack. In much the same way as a car is assigned an identity number and registration plate at the point of manufacture, drugs will be required to have a unique, machine-readable code that can be used at any given point in the supply chain to help to verify its authenticity

All activities related to drug serialisation that are evolving in different countries are backed by the overarching global initiative managed under the auspices of the WHO. It set up the International Medical Products Anti-Counterfeiting Taskforce (IMPACT) which developed principles and elements for national legislation against counterfeit medical products.1 Be it the EU Falsified Medicines Directive (FMD), Brazil's ANVISA, Argentina's ANMAT, South Korea's MHW, China's SFDA, or the recently announced senate bill (Drug Quality and Security Bill) in the USA, manufacturers subject to any of these schemes are now engaged in a race against time to implement serialisation ahead of the deadline. This applies to all products supplied into the respective territories and not just to locally-produced drugs or indigenous manufacturers. Taking the EU FMD as an example, the timeline for compliance is three years after the forthcoming publication of the Delegated Acts in each of the EU28 countries. For all but three of these countries, the date for full compliance is expected to be 2017.

The Directive applies to all branches of the industry including research-based manufacturers, generics producers, contract packers, parallel traders' importers, wholesalers and distributors. Simply put, any organisation intending to supply Prescription Only Medicine (POM) and some Over-The-Counter (OTC) products into the EU which after that date will not be able to do so unless full compliance can be demonstrated.

There is a view, apparently relatively widely-held, that the challenge of item-level serialisation does not extend beyond the confines of the packaging hall. This may stem from the fact that the most obvious expression is on-pack information in the form of a code, which has of course been required for both legislative and GMP purposes for many years.

However, serialisation is a significant shift in that data will be unique to each pack rather than to each batch. This has huge knock-on effects beyond the installation of new equipment, namely, on the need for increased staff investment and stakeholder engagement. To characterise it as an engineering issue is therefore to grossly underestimate its consequences, which touch virtually every business function in pharmaceutical manufacturing.

This white paper looks at the challenges encountered during serialisation trials by the 'early adopters' and provides guidance on strategies to overcome them. Most trials were undertaken at a time before any legislative imperative or global standards and although these trials have not gone the full extent of serialisation and aggregation, the lessons learnt may prove invaluable.

It is worth noting at the outset that the first challenge of serialisation is the fact there is not a 'one size fits all' solution. No one supplier will be able to handle all the requirements, from the coding and marking technology to the data handling. Even reportedly 'turn-key' or 'endto-end' solutions will inevitably be comprised of multiple vendors working in collaboration

Technology

For packaging manufacturers, the updating of lines and installation of serialisation-capable coding equipment may seem like a project much like any other, with predictable timelines and considerations such as where the coding and inspection equipment will be located and how it will be integrated. This may be true to some extent, but it is an assumption that merely scratches the surface: trials have shown that installing and commissioning serialisation-ready equipment is markedly more complex.

There is also likely to be a debate about which coding technology is best suited to serialisation. By now manufacturers should be well aware that older technology such as hot foil or embossing is now far beyond its expiry date. Serialisation-capable alternatives might include thermal ink jet (TIJ), laser or thermal transfer overprint (TTO). Variables such as substrates, speeds and pack design might need to be factored in, as does any company-specific preference based on legacy technology, plant location and experience.

Whatever the equipment choice, manufacturers should certainly not be delaying their serialisation projects while waiting for clarification of all the finer details of whichever legislative scheme (or schemes) applies to them. There is sufficient detail and guidance already available for the industry to make informed decisions about how to achieve unique pack identification. With the exception of China (which is looking at the option of linear barcodes), the model is a combination of a 2D data matrix code and human readable text. Thermal ink jet and laser are a good choice as because codes need to be verified as well as applied, print quality is a critical factor.

Furthermore, although data matrix codes are designed with inherent redundancy, the scrutiny of text by vision systems is less forgiving, so high levels of consistency need to be achieved in order to avoid rejection. While the lower resolution of CIJ is more than sufficient for alphanumeric data, it is not recommended where small, high-density codes need to be applied and verified, leaving thermal ink jet and laser as the systems of choice.

Laser offers significantly lower running costs because the only consumables are the filter bags for the extractor and may therefore be the preferred route in instances where throughputs (and hence potential ink consumption) are high; laser marking is also indelible and therefore a good choice for cold chain products. Thermal ink jet offers a clarity and density of marking combined with a lower initial capital outlay and may therefore be a better option for other applications.

Both offer the speed and quality of marking required in a high-speed serialisation environment and both are capable of meeting the requirements of all pharmaceutical traceability schemes in operation or planned around the world, which will certainly be a consideration for manufacturers supplying multiple regions from a single plant.

With any ink-based marking system, the quality of the end result relies as much upon the choice of ink as it does on the capabilities of the printer and the type of product packaging. The advent of serialisation and the associated volumes of data required to be applied to each pack has spurred new developments in multi-substrate inks for TIJ printers, which offer fast drying times (essential to prevent smearing where tamper evident labels are applied as part of a high speed packaging operation), optimised clarity to minimise the incidence of false rejects produced by machine vision systems and enhanced lightfastness so that the code contrast remains high from the point of production, to dispense and beyond.

Data

According to IBM, we now generate 2.5 quintillion bytes of data every day – to the extent that 90% of the data in the world today has been created in the last two years alone. Those who have experimented with serialisation thus far are well aware of just how much data it can create and the challenges associated with storing and maintaining the integrity of that data for the required period of time.

The volume of data generated by serialisation derives principally from the fact that each item now consists of two parts – a physical asset and a data asset – and that the association between the two must remain linked from the moment a unique identity is assigned to a pack right through to the moment it reaches the patient. Delve deeper and it quickly becomes clear that this simple fact alone will require a modal shift in the manufacturing mind-set, with each pack effectively a unique batch of one. Reconciliation, which has until now been a line side task completed once per batch, will in future need to extend right through the supply chain and be open to interrogation for the life of the product and beyond.

The outcome here is that product data must be uploaded to a national or supra-national systems infrastructure against which product IDs will be verified at the point of sale or dispensing. This in turn raises the question of data aggregation (the establishment of hierarchical relationships at each stage of the packaging process). While some of the schemes in play include aggregation as a requirement, others do not. However, it would seem to be a logical extension of item-level serialisation, enabling, for example, the data for each pack in each case, and each bundle on a particular pallet to be retrieved with a single scan. It is therefore a requirement which manufacturers would do well to accommodate, even if not implemented from the outset.

The same principles apply to equipment capabilities for aggregation as they do for serialisation: printers need to have on-board capability to apply unique information to each aggregated 'unit'. Establishing hierarchical associations between the unit-of-sale packs in a bundle, bundles in a case, cases in a pallet and so on enables any party authorised to handle product in its journey through the supply chain to interrogate, with a single scan, precisely which items the batch contains.

While speed is not such a significant requirement in code application at aggregation stage, quality and legibility most certainly are: as stated above, a pallet code is effectively the key to the unique data associated with every single item on that pallet and the consequences of a failed scan are therefore significant. As at item level, users have a choice of technologies, the principal ones being print and apply labelling machines or, for printing direct onto the packaging, large character continuous ink jet systems offer a label-free solution.

There is currently no protocol for uploading data to a central repository and to date, it remains unclear how data will need to be supplied to regulators and what the obligations are on the manufacturer to replicate and retain that information and for how long. The strategy will vary from one company to the next but the planning process needs to start now, before the deluge begins.

Re-designing packaging protocols

One of the questions thrown up by serialisation is whether a machine readable code is artwork or data. Until now, any pre-printed code, such as a GTIN, would have been treated as artwork by some; however, since it will now form part of the product identity, there is an extremely strong case for re-classifying all codes as data and storing them accordingly. The need to maintain a unique data asset in parallel with each physical pack will place restrictions on the way packaging operations might traditionally have operated: if a pack is rejected or otherwise removed, how is it removed from the database and what strategies are in place to ensure that the integrity of serialisation regimes is uncompromised by such events? How will rework of false reject products be managed in the future? The concerns for manufacturers of both research based and non-researched based pharmaceuticals are self-evident.

Although daunting, there are positives to the creation of such a database: engineers on the packaging hall floor will have access to the database, and if there are issues on a line, the database can be used to pinpoint to certain packs, when they were produced, and if they caused any problems. This will drive up standards and may create leaner production lines.

A new status quo in operating efficiency

According to the early adopters of serialisation, the engineering challenge lies in returning to 'business as usual' in terms of operating efficiency. Although manufacturers are no doubt anticipating an impact, it is crucial to be aware early on that the effect is considerable. One company reported serialisation at 300 units per minute as comfortable, 400 to 450 per minute achievable but not fully robust, and 500 per minute and beyond still a real technical challenge. Anecdotal evidence also suggests that the reject/re-work level in the early stages can be as much as 10%, far above what is normally acceptable. This reduces over time, with rates well below 1% being achievable but it takes commitment, effort and engineering knowhow. In many cases rejects bins in the packaging halls simply are not big enough; this might seem like an almost trivial concern but if a full reject bin results in an unplanned line stoppage, then it is a point that needs addressing.

The best possible foundation for robust serialisation is uninterrupted production: it will quickly become apparent that unplanned stoppages due to below par line performance cause significant and unacceptable headaches in a serialised environment. The causes will need to be identified and addressed as a matter of urgency if acceptable operating efficiencies are to be achieved. Good practice, such as planned and pre-emptive maintenance to ensure lines are fit for serialisation ahead of time will ensure that businesses can concentrate on the more significant and less familiar challenges as the deadline approaches. Investment in staff The challenges demonstrated in this paper so far will largely need to be addressed and solved by engineers. Manufacturers need to ensure that their staff members are confident in dealing with issues that are not currently in their remit. Investment in training, therefore, is crucial. Budgets should be assigned now to get engineers trained and ready to help get lines back to 'business as usual' as quickly as possible. Implementing serialisation highlights any flaws on a packaging line. Issues taking longer to resolve can cut quite significantly into overall equipment effectiveness and profit margins. Training will limit the times it takes to overcome problems, and though it may seem an unnecessary expense, it can up morale during a challenging period, lead to new best practice and drive up standards across the organisation.

Stakeholders

Trials to date have shown that overcoming the challenges detailed so far becomes a lot easier with stakeholder buy-in. But as production, regulatory compliance and quality assurance personnel know, this is not always as easy to attain. Many stakeholders believe serialisation to be a purely engineering challenge, but this seriously underestimates its impact right across the business. Project engineering new equipment into existing lines is the essential first step confined to the packaging hall, but beyond that the critical success factor is senior stakeholder engagement to establish a robust serialisation infrastructure. The engineering challenge of recognising that each physical pack has an associated data asset, and that association must remain intact throughout the supply chain, is easier to overcome with support from the top.

As a result, manufacturing managers need to be in constant communication with stakeholders to ensure buy-in way ahead of the deadline. This case is strengthened considerably by the widespread view that serialisation will be a key element of future brand protection schemes. The impending legislative imperative aside, serialisation has the potential to improve the supplier-patient relationship across the industry. Patients will also be able to verify the authenticity of their medicines, increasing trust in the brand and the manufacturer. That confidence might well lead to improved patient compliance, resulting in better outcomes.

Business Benefits

Implementing such a significant change in a relatively short timescale and in an industry as highly-regulated as pharmaceuticals is a daunting prospect and it is therefore no surprise that much of the focus currently is on problems and challenges. At the most basic level, many are approaching serialisation projects with caution and asking what the regulations mean for their business. This, inevitably, leads to a 'wait and see' approach, before investing in new plant and equipment. The trick, in many ways, is to be more visionary. By taking a front-foot approach, manufacturers and packers can have their say in defining standards and formulating the regulations at an early stage. At a company level, by adopting a robust approach to the new regulations, companies can get ahead of the curve through improved response to counterfeiting incidences, reducing their prevalence and the risk of contamination. It also works to enhance the safety profile of marketed products, with the unique on-pack data serving as a guarantee of authenticity and quality. Although this might seem a distant prospect right now, serialisation ultimately offers the opportunity to really drive down business costs. By improving operating efficiencies, reducing inventory losses, improving the rate of returns, recalls and the chargeback process, and providing all-round visibility of the supply chain, the pharmaceutical business can substantially improve its outlook, in terms of efficiency, profitability and brand image.

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