White Paper

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A Guide to Pharmaceutical Serialisation

Choosing the Right Equipment Supplier

METTLER TOLEDO

Contents

1 Introduction

In the light that the world is facing a persistent and increasing threat from counterfeit, mis-branded, adulterated, or diverted prescription drugs, government leaders, politicians and executives from major pharmaceutical providers are driving efforts to develop methods to reliably track and trace prescription drugs.

Based on this growing threat, many countries have started to address vulnerabilities in the supply chain by enacting legislation which, among other things, requires a comprehensive system, most often referred to as serialisation or in the United States as e-Pedigree (electronic pedigree).

This growing movement towards utilising serialisation to track drugs will inevitably lead to companies found to be receiving or sending unserialised drug shipments opening themselves up to fines, orders to discontinue operations or even criminal investigation.

The following paper provides companies in accordance with current or emerging serialisation legislation critical information on making an implementation decision by:

- Summarising the minimum requirements of a serialisation solution
- Outlining the complexity involved when implementing a serialisation solution
- Detailing questions that must be addressed when choosing a production line equipment supplier

Most pharmaceutical companies have already started to focus on implementing a serialisation strategy and defining their needs on trusted partners with production line serialisation solutions. All pharmaceutical companies will be affected by serialisation regulations. It is not an option to take a wait and see approach.

"According to the World Health Organization, 10% of the world's pharmaceuticals are counterfeit and as much as 1-2% in the USA. If we consider the rate of counterfeiting in the US at just 1% of the estimated 3.4 billion prescriptions in 2007, over 34 million counterfeit prescriptions were consumed in the US."

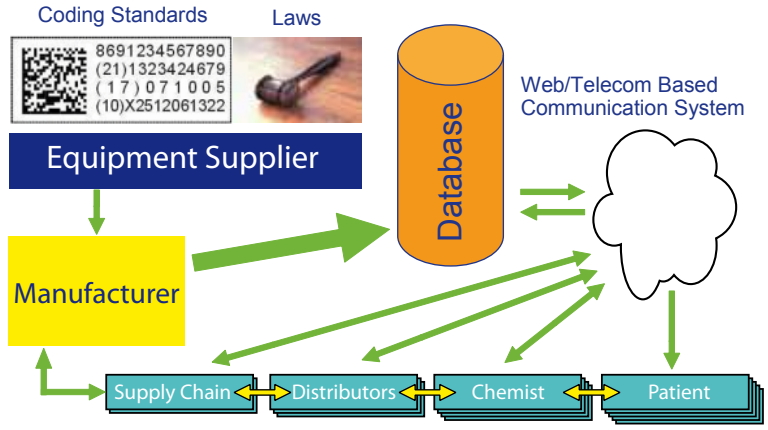
It is statements and findings like these that are raising concerns over the control of pharmaceuticals in the supply chain.

2 The Basics of Serialisation

The basic idea behind serialisation is very easy to understand but very difficult to implement in the manufacturing process. It requires a comprehensive system to track and trace the passage of prescription drugs through the entire supply chain.

The vast majority of prescription drugs received by patients are safe. However, given the number of potential players in the supply chain and the differences in regulations and laws world wide covering each of them, opportunities do exist for dangerous counterfeit and adulterated drugs to be introduced into supply.

In an effort to combat this risk of counterfeit and adulterated drugs, national regulators have pursued the need for serialisation. A complete serialisation programme represents the complete history of a given product's chain of custody from the manufacturer to the point of dispensing. Much of the early work around implementing solutions has focused on support of serialisation using electronic solutions, both in terms of applications for managing serialisation data, printing of human readable markings and sensory technologies for verifying this marking. While there are many advantages in early implementation of a serialisation programme there is still much confusion as to how laws and regulations will evolve in the future.



Example of a Serialisation Programme

Pharmaceutical manufacturers are investing in ways to uniquely serialise each unit and to register the parent child relationships of units into larger containers, cases or cartons and even up to pallets.

The information required in a serialisation programme is strongly dependant on the many different laws and standards. Typical information could include some or all of the following:

- The complete supply chain ownership information from the manufacturer all the way down to the pharmacy from which the prescription drug was handed out to the patient
- Detailed information for each person who certified delivery and receipt of the prescription drug including company, name and address
- The name of the prescription drug, its quantity, its dosage form and strength
- The date of each transaction in its distribution.
- The sales invoice number(s) for each transaction
- The number of containers for each transaction
- The expiry dates and the lot/batch number(s)
- Complete shipping information
- A certification that the information is true and accurate

3 Minimum Serialisation Implementation Requirements

While the long-term requirements around serialisation are still uncertain, the ability to track a specific drug product through the supply chain and trace its exact journey will help secure the integrity of the drug supply by providing accurate documentation. The minimum requirements for a complete serialisation programme also varies from country to country and could include one or all of the following points:

- Authentication and certification of each owner of a prescription drug from the current owner back to the original manufacturer
- Validation that serialisation data matches the physical product received
- The means to check that all prescription drugs in stock have been serialised
- Association of serialisation information when despatching products
- Confirmation that products have complete and accurate documentation

Only an automated electronic solution will be able to meet these requirements. These solutions need to be designed, implemented and operated to address the unique challenges they present. Such an automated electronic solution will lead to very large amounts of data which will need to be shared with all trading partners. Some of these challenges include:

- **Data Volumes:** Serialisation data will require a significant increase in the data volumes shared between trading partners
- **Information Storage:** Each player in the supply chain will need to maintain complete and accurate records of all items back to the manufacturer for multiple years
- **Reliability:** Serialisation information must be available before a product can be despatched.
- **Certification:** Each person in the supply chain must be able to authenticate the chain of custody back to the manufacturer, maintain a record of this authentication, and certify that the shipments have complete and accurate documentation

No matter how and when serialisation laws are implemented, all pharmaceutical manufacturers, distributors and retailers must be ready to comply and be ready to address these technological challenges.

4 Complexity

There are several factors that influence the total complexity, risk and cost of implementing and managing serialisation solutions, including regulatory uncertainty, technological evolution, and infrastructure requirements.

Driving much of the complexity around creating and managing serialisation programmes is the complexity of the pharmaceutical supply chain itself. It is unique in its complexity and reach. Prescription drugs are distributed to every corner of the world. Drugs are produced, distributed, repacked and sold by hundreds of thousands of organisations working in concert to ensure every patient gets the drugs they need. This complexity creates many questions about how best to address serialisation and how it will affect the supply chain and distribution channels.

Regulatory Uncertainty: There are many unanswered questions regarding serialisation requirements even though the first significant laws came into effect in 2006:

- Will existing national law need to be changed?
- Will serialisation be required from all countries?
- Will there be a global standard?

Requirements in 18 months may be significantly different than they are today. For example, the industry has already started to mass serialise drugs and there are already standards and concepts being implemented in Europe and the world today. Some current worldwide serialisation initiatives are shown below:

- **Turkey** – GTIN, serial number, LOT and EXP date marked on the product
- **France** – Vignette label, product number (CIP) and LOT/EXP with Datamatrix Code
- **EFPIA concept** – The harmonization of pharmaceutical products codification throughout Europe via serialized Datamatrix Code
- **E-Pedigree Law California** – electronic pedigree to track and trace prescription drugs through entire supply chain: Timeline 01.01.2015 or later

It is not foreseeable if one system will be adopted as the global standard or if each continent will have its own standard. At present all models are in the running. Frequent technology updates are likely. Existing laws will need to be changed as the regulatory bodies get experience with their laws to close loop holes. These laws will require changes to the underlying software and production equipment supporting serialisation compliance. The cost of upgrading is a major concern in determining the total cost of production. Initial implementation and investment cost are also an issue; will the equipment you buy today be able to comply with future serialisation requirements and laws?

5 Choosing the Right Production Line Equipment Supplier

Given regulatory uncertainty, technological evolution, and infrastructure requirements, early adopters are establishing long-term relationships with strong partners who can help manage costs and minimise risks. Some of the points which need consideration include:

- How informed is the partner with current regulatory requirements? This is important to ensure required functionality is available in the solution and also ensures that the partner will be a valuable contributor in longer term strategic initiatives
- Is the partner able to supply solutions using tried and trusted components and technologies already in use in your production line? This will save considerable integration costs and time.
- Has the partner demonstrated the performance needed to meet the requirements?
- Does the partner have the financial stability and resources to meet near-term requirements and to deliver an economical service in the long-term?
- Does the partner have global service and support strategically located for rapid response when needed on site?
- Has the partner solutions which are flexible enough to integrate your current software and hardware requirements including the ability to easily incorporate new features as technology and requirements evolve?

Laser Marking, Camera Verification and Checkweighing:
A Serialisation Solution for the Production Line

There are many critical factors which need to be addressed when choosing a serialisation equipment supplier. Here we will take a quick look at the 3 types of specialist equipment components essential for the physical serialisation of pharmaceutical products.

Camera Equipment: The camera system receives the serialisation data from the central database, gives this information to the printer and then examines the package marking to verify that the marking is legible and correct before signalling back to the central data base that the serial number has been allotted. Your supplier should be able to integrate the camera soft and hardware of your choice to minimise integration issues.

Printing Equipment: This can be done using an ink jet printer or laser marker directly onto the packaging, or by using a labeller. Once again it is important to use printing solutions of your choice which could already be in use on your production line and fulfil the printing requirements.

Checkweighing Equipment: This ensures that the contents of each package, as marked and verified, are present and that each package is complete. On or directly before the checkweigher is also normally the best location to place your serialisation marking and verifying equipment to keep critical quality control points to a minimum.

The software solution for management of internal and external databases is also a critical consideration for all installations and must be flexible enough for adaptation to future requirements.

For each of these specialist equipment types there are a great many potential suppliers who, individually, will be able to meet your requirements for their single component but may cause significant integration problems when being combined with the other equipment types. It is strongly advised that you choose one central supplier who already has successful partnerships with the other equipment suppliers and has experience in combining marking, visual verification and checkweighing components in one complete serialisation system.

Using a complete solution supplier has many undeniable advantages and benefits:

- One point of contact for all three systems
- Quicker project realisation from order to delivery
- Component compatibility assurance
- Combined systems are more compact allowing easier line integration and have fewer moving parts reducing maintenance time and effort
- Reduction of user interfaces reduces operation errors and makes product changeover faster and more efficient reducing downtime

6 Post Serialisation

Investing now in serialisation related infrastructure goes beyond compliance. It should be considered as an overall strategy of supply chain safety, security, and efficiency. While safety is a major factor, the cost of delivering pharmaceuticals is also of great concern. It is essential for all pharmaceutical supply chains to supply the right quantity of the right product at the right place at the right time – as the cost and consequences of not achieving this goal are extremely high. Chain of custody technology can be a key factor in improving customer service and satisfaction.

At METTLER TOLEDO Garvens, we believe that our customers should pursue a strategy and make investments that not only accomplish regulatory compliance but also establish a foundation for strategic value.

7 FAQs

What is the danger in taking a "wait and see" approach until technology, standards and legislation mature?

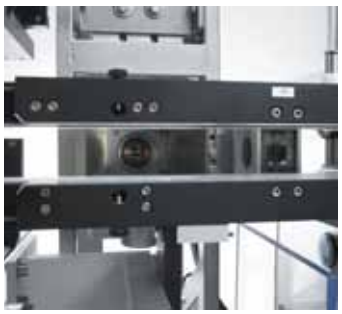
The danger in taking a "wait and see" approach is already becoming very visible. Patients are being harmed by counterfeit pharmaceutical products and the industry is losing the public's trust in the supply chain. Industry members now taking the lead in serialisation development will be able to influence regulatory legislation and standards which will be imposed on the rest of the industry.

How do I handle the evolving legislative serialisation landscape?

Ensure that you have well functioning communication procedures between your company and the governing authorities to ensure that when new legislation is passed or old legislation is changed that you are timely informed of all current and pending requirements. Also ensure that your production line equipment suppliers have a similar procedure and have created a solution flexible enough to take into account possible future changes.

If I have a functioning checkweigher, does it make sense to replace this checkweigher with a complete new checkweighing system with integrated serialisation components?

As a general rule most pharmaceutical companies already have a perfectly adequate checkweigher and need only to integrate a marking and verification solution (M&V) within the production line. In cases where there is a real shortage of floor space for the integration of a stand-alone M&V solution you may want to consider procuring a combination solution which has the same dimensions as your current checkweigher. The benefits of a complete system are clear and include simpler line integration, assurance that all components will work together and only one point of contact for service and support matters.



Will integrating a marking and verifying system have a negative effect on my OEE?

Introducing any new piece of production line equipment can have a negative influence on your OEE. To ensure that this is not the case you must be careful to choose equipment suppliers who are competent at processing difficult to handle products at high throughput. Slowing down your production line is not an option. Look for solutions which have line speeds of at least 90 m/min. This will enable you to maintain current throughput levels and give room for future speed increases. Safe and smooth product transfer especially onto the system and precise transportation of the product in front of the printer and camera are critical in ensuring a good printing quality and best possible marking verification. Imprecise product handling will lead to an increase in rejected products and could lead to back ups and jams which will inevitably cause and increase downtime occurrences. Your production line equipment supplier should understand OEE and should be able to supply solutions which will not negatively affect it.

I want to replace my checkweigher with a complete combination system but my product line equipment supplier cannot integrate the camera or printing system of my choice, is this normal?

It is perfectly normal for you as customer, to define the system components you have had experience with in the past and to expect them to be integrated into a complete combination system. The companies who supply camera and printing systems work with all combination system suppliers who understand their technology and have proven that they can readily integrate these into a combination solution system. Look for a production line equipment supplier who works with all the world leading pharmaceutical camera and printing equipment suppliers, especially the systems of your choice, as they will have a solution for you.

What is the best approach for many different production lines in different countries?

A flexible standard approach is the best for this type of problem. Although it is always better to have a standard solution which can be deployed world wide this is not always possible. Because of different production line requirements which could involve floor space availability, software requirements, variety of camera and printing equipment and local laws and regulations one product will probably not fit all. Good production line equipment suppliers will be able to help you with global project management, advice and support. They will be able to supply a standard solution which will satisfy the requirements for the majority of production lines, be able to suggest where it would make sense to change local conditions to allow for the standard solution and also have enough flexibility to offer bespoke solutions where the standard solution is not possible.

Notes

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