A Guide to Pharmaceutical Serialization
Choosing the Right Equipment Supplier

Trust Hi-Speed to show you the way

Mettler Toledo
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1 Introduction

In the light that the world is facing a persistent and increasing threat from counterfeit, misbranded, 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 serialization or in the United States as e-Pedigree (electronic pedigree).

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

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

- Summarizing the minimum requirements of a serialization solution
- Outlining the complexity involved when implementing a serialization solution
- Detailed questions that must be addressed when choosing a production line equipment supplier

Most pharmaceutical companies have already started to focus on implementing a serialization strategy and defining their needs on trusted partners with production line serialization solutions. All pharmaceutical companies will be affected by serialization regulations. It is not an option to “wait and see” it's imperative to be a leader in the industry.

Counterfeit pharmaceutical products will cost the industry an estimated $75 billion in sales by 2010

(Source: Center for Medicines in the Public Interest)
2 The Basics of Serialization

The basic idea behind serialization 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 worldwide 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 serialization. A complete serialization program 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 serialization using electronic solutions, both in terms of applications for managing serialization data, printing of human readable markings and sensory technologies for verifying this marking. While there are many advantages in early implementation of a serialization program there is still much confusion as to how laws and regulations will evolve in the future.

Pharmaceutical manufacturers are investing in ways to uniquely serialize 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 serialization program 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 expiration dates and the lot/batch number(s)
- Complete shipping information
- A certification that the information is true and accurate
3 Minimum Serialization Implementation

Requirements

While the long-term requirements around serialization 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 serialization program also vary 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 serialization data matches the physical product received
- The means to check that all prescription drugs in stock have been serialised
- Association of serialization 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:** Serialization 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:** Serialization 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 serialization 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 serialization solutions, including regulatory uncertainty, technological evolution, and infrastructure requirements.

Driving much of the complexity around creating and managing serialization programs 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 organizations working in concert to ensure every patient gets the drugs they need. This complexity creates many questions about how best to address serialization and how it will affect the supply chain and distribution channels.

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

- Will existing national law need to be changed?
- Will serialization 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 serialize drugs and there are already standards and concepts being implemented in Europe and the world today. Some current worldwide serialization 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 January 1, 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 serialization 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 serialization requirements and laws?
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 minimize 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?
- Does the partner solutions have the flexibility to integrate your current software and hardware requirements including the ability to incorporate new features as technology and requirements evolve?
There are many critical factors which need to be addressed when choosing a serialization equipment supplier. Take a quick look at the three types of specialized equipment components essential for the physical serialization of pharmaceutical products.

**Vision Equipment:** The vision system receives the serialization data from the central database, sends the information to the printer and examines the package marking to verify that the marking is legible and correct before signalling back to the central database that the serial number has been allotted. Your supplier should be able to integrate the vision software and hardware of your choice to minimize integration issues.

**Printing Equipment:** This can be done using an ink jet printer or laser marker which prints 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 place 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. It is ideal to place serialization marking and verifying equipment on or directly before the checkweigher to maximize critical quality control points.

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

For each of these specialized 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 serialization system.

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

- One point of contact for all three systems
- Quicker project realization 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 therefore reducing downtime
6 Post Serialization

Investing now in a serialization 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 HI-SPEED, 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 are taking the lead in serialization development and 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 serialization 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 serialization 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.
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 (Overall Equipment Effectiveness). 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 vision inspection are critical in ensuring good printing quality and the best possible marking verification. Imprecise product handling will lead to an increase in rejected products and could lead to backups 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 have a negative effect.

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

It is perfectly normal for you, as a 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 vision inspection 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 vision inspection 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 worldwide this is not always possible. Because of different production line requirements which could involve floor space availability, software requirements, variety of vision inspection 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 and 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 specialized solutions where the standard solution is not possible.