Fighting the battle against drug counterfeiting
How technology can assist

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Learn how Rockwell Automation’s serialization solution helps to introduce the concept of mass serialization
Drug Counterfeiting - A global public health challenge

Drug counterfeiting is a twofold problem. There is an economic impact, but much more concerning there is an increasing threat for the safety of the patient population.

The economic burden of drug counterfeiting is continuously increasing but beside the economic dimension, counterfeit drugs could have severe harmful effects on patients. The use of counterfeit medicines may lead to adverse reactions, therapeutic failure or drug resistance. (Note here we refer to bad / poisonous materials, substandard drugs and bad combinations).

So-called “Spurious/falsely-labeled/falsified/counterfeit (SFFC)” medicines are medicines that are deliberately and fraudulently mislabeled with respect to identity and/or source.

The following table gives an example of SFFC medicines.

<table>
<thead>
<tr>
<th>SFFC medicine</th>
<th>Country/Year</th>
<th>Report</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-diabetic traditional medicine (used to lower blood sugar)</td>
<td>China, 2009</td>
<td>Contained six times the normal dose of glibenclamide (two people died, nine people hospitalized)³</td>
</tr>
<tr>
<td>Metakeffin (antimalarial)</td>
<td>United Republic of Tanzania, 2009</td>
<td>Discovered in 40 pharmacies: lacked sufficient active ingredient²</td>
</tr>
<tr>
<td>Viagra &amp; Cialis (for erectile dysfunction)</td>
<td>Thailand, 2008</td>
<td>Smuggled into Thailand from an unknown source in an unknown country³</td>
</tr>
<tr>
<td>Xenical (for fighting obesity)</td>
<td>United States of America, 2007</td>
<td>Contained no active ingredient and sold via internet sites operated outside the USA⁴</td>
</tr>
<tr>
<td>Zyprexa (for treating bipolar disorder and schizophrenia)</td>
<td>United Kingdom, 2007</td>
<td>Detected in the legal supply chain: lacked sufficient active ingredient⁵</td>
</tr>
<tr>
<td>Lipitor (for lowering cholesterol)</td>
<td>United Kingdom, 2006</td>
<td>Detected in the legal supply chain: lacked sufficient active ingredient⁶</td>
</tr>
</tbody>
</table>


Counterfeiting is a world-wide problem. It is not limited to certain types of products or 3rd world countries. Lack of supervision and a more and more competitive market has provided a platform being insensitive to counterfeit medicines in all parts of the world.

**Economic damage**

On top of the impact on patient’s health there’s a dramatic economic dimension. Companies are losing a significant amount of products which are stolen, copied and re-sold on the black market. Having no chance to identify those products as being stolen and thus preventing reselling them hits the companies twice: once by financial losses and twice by damaging their reputation on the market.
Starting the fight

The WHO (World Health Organization) has summarized the need to focus on the following key areas:

- Legislative and regulatory infrastructure to provide a strong framework to empower regulators, police, customs officials and the judiciary
- Regulatory implementation and enforcement of the new framework
- Communication to increase the awareness of the risks created by counterfeit drugs
- Technology to prevent, deter or detect counterfeit medicinal products

First implementations to fight drug counterfeiting with technology-based solutions are present on the market. The first solutions support the recording, tracking and communication of a drug pedigree where this white paper is about.

As a further perspective the focus of forthcoming initiatives will probably be to ensure that on top of the uniqueness the integrity of the original package is absolutely guaranteed throughout the entire supply chain, from the time it leaves the original manufacturer to the point that it reaches the end user. This could be achieved by using special seals, tamper evident labels and similar technologies.

Thus, product serialization will be just one component preventing counterfeits – there will be more to come.

Current regulations

The following map describes the worldwide roadmap for introducing serialization as one measure against counterfeiting. As one can see, there is no common approach across different countries, which makes it even more difficult for the pharmaceutical industry to provide a global answer to the problem.

Source: www.pharmaserialisation.com

Knowing this it becomes also even more important for solution providers like Rockwell Automation to develop a flexible and scalable solution that will be able to provide the right approach to the complex regulatory needs.
What is a drug pedigree?

A drug’s pedigree represents the complete history of a given product’s chain of custody, from the manufacturer to the point of dispensing.

The term "e-pedigree" means an auditable electronic record of every step taken by a retail package of prescription drugs as it moves from the factory to the final point of sale. This chain-of-custody record will be used to assure the integrity and safety of the nation’s drug supply.

The challenges around the creation and tracking of an ePedigree document can be categorized as follows:

- Serialization
- Creation of an initial ePedigree
- Tracking of an ePedigree across the supply chain

Serialization

Serialization is the process of creating uniqueness for retail items. This will be managed by marking each individual item with a unique identifying code. To carry this information, two methods can be considered:

- Applying a RFID (Radio-Frequency Identifier)
- Printing of a barcode (usually a 2d datamatrix code)

Both methods allow reading the information with a scanner, which is the foundation to track the material from his birthplace, down to the place of consumption.

The fact, that there are still multiple weaknesses in the RFID technology, like cost, privacy concerns, and technical limitations has as consequence that barcode solutions are in favour.

Especially two dimensional barcode labels provide the capability to hold the needed information.

The serialization process reveals as series of challenges:

- **Guarantee of uniqueness of applied numbers** – The industry must provide a global schema that allows each manufacturer to apply a worldwide unique number. These challenges become even bigger by preferring randomized numbers making prediction of used serial numbers by counterfeiters almost impossible.

- **Applying and reading barcodes** - All players need the capability to verify, create, and apply barcodes in their environment.

- **Physical product limitations** – Small retail items with limited space for holding barcodes like pre-filled syringes and vials create another level of challenges. Different packaging materials like glass, cartons or plastic make it even more difficult.

- **Printing and verification in a high speed environment** – Today’s packaging machines are using production rates up to 500 units per minute. Packaging lines are prone to dust and vibration which leads to an even more challenging environment for printing barcodes in high quality and for verifying codes.
Creation of an initial ePedigree

The first key element of the ePedigree process is the creation of the initial ePedigree document. This element is the first documented proof by a manufacturer of what has been produced on an item level.

Beside fundamental product information like product name, product number, batch number, expiry date, the initial ePedigree holds additional information of each individual retail item and its unique number. Furthermore, this document indicates as well, what the complete packaging structure looks like in terms of: which retail item went into which shipper box onto which pallet. This process is usually known as aggregation.

Challenges are notably seen in the area of information management.

- **Linking different data repositories** – Context information of production are often held in the ERP (Enterprise Resource Planning) system or part of plant level MES (Manufacturing Execution System) solutions. These systems are usually designed to track products on a production batch level. The needed tracking capabilities on item level require added functionality or new concepts in production management.

- **Storage of nesting information** – The information of the packaging structure describing which box and which shipper case went into which shipper and onto which pallet is often referred as nesting information or aggregation. Creation, verification and storage can be challenging.

Systems to maintain these data need to provide capabilities to hold and change the aggregation information under the regulatory framework of 21 CFR Part 11. The design of such data containers needs to reflect the ultimate purpose of querying the data as well.

Tracking of an ePedigree across the supply chain

At a long term vision each party in the supply chain of prescription drugs is required to provide pedigrees to the recipients of those drugs.

That includes a certification of the originating party that the product is authentic and requires to the necessity that recipients of products authenticate each previous transaction in the pedigree and add their own certification of receipt and authentication to the pedigree.

These are some of the challenges the industry faces:

- **Availability of technical infrastructure** – All players in the supply chain have to authenticate, track and certify pedigrees. All players need the appropriate infrastructure of barcode scanning, data maintenance and data access.

- **Information storage** – All players need to maintain complete, accurate, and secure records of drug pedigrees for multiple years.

- **Privacy and ownership of logistical data** – The tracking of pedigree information creates an extensive repository of business critical selling data for each individual product and brand. There is a need for a clear ownership concept to protect the data against use with criminal intent.

- **Transaction volumes** – The amount of data to be handled will be massive. This is comparable with banking transactions, which create trillions of records per year.

- **Process security** – It must be absolutely guaranteed that no invalid retail item enters the supply chain; invalidity could result (out of many) from
  - An unreadable or even wrong barcode or a mismatch between barcode content and human readable text beneath the barcode,
  - Non uniqueness of serial numbers or
  - Mixing of items from different package lines.
Eliminating human errors by providing the respective process security is one key challenge in the serialization context.

**GS1 Standards**

The GS1 system of standards is the most widely used supply chain standards system in the world (see [www.gs1.org](http://www.gs1.org)). Rockwell Automation is GS1 Solution Provider:

Rockwell Automation supports GS1 standards like:

- GS1 Identification Keys (GTIN, EPC etc.)
- GS1 Bar Codes (GS1-128, GS1 Data Matrix etc.)
- GS1 EPCglobal

**Serialization – Benefits beyond compliance**

Beside the pure fight against counterfeit drugs, item serialization and item tracking throughout the supply chain provides a series of additional benefits, which should be considered.

Those benefits include:

- **Improved product safety** - reduction in theft/loss/pilferage, track and trace technology enables instant product recall notification and provides the electronic basis for dramatic reductions in dispensing errors to be cut dramatically by enabling product to be checked prior to dispensing
- **Improved inventory management** - reduction in excess inventory, increase in reported on-time delivery
- **Improved supply chain visibility** - increase in access to supply chain data, increase in timeliness of shipping information
- **Improved product handling** - increase in automated handling of goods
- **Process improvements** - reduction in process deviations
- **More efficient customs clearance process** - reduction in cargo delays, reduction in cargo inspections/examinations
- **Speed improvements** - reduction in transit time, reduction in delivery time window
- **Resilience** - reduction in problem identification time, response time to problems, and in problem resolution time
As a leading solution provider to the Life Sciences industry, Rockwell Automation is committed to support the industry in managing the challenges of implementing a technical solution for serialization leading to a complete ePedigree.

The serialization landscape can be structured in 4 layers:

- **Shop floor layer** - This is where the initial ePedigree data is created and the manufactured goods are stamped with serialized labels or tags. Any aggregation level (folder cartons – bundles – cartons – packages – containers – etc.) is also recorded here.

- **Plant layer** - Since a single plant can contain several shop floor levels, pedigree information of each shop floor is collected and administered here.

- **Internal supply chain (Enterprise) layer** - Shipping products between plants for further distribution process is recorded here.

- **External supply chain layer** - Finally the drugs are delivered to distributors, wholesalers or pharmacists and hospitals directly. This process is recorded here.

Rockwell Automation’s serialization solution addresses especially the challenges on the shop floor and plant layer. It is an add-on concept that can be easily integrated into existing line configuration or could be an essential part for new packaging lines.
Rockwell Automation’s serialization solution connects all IT levels and basically provides three main components:

1. **Site Controller**
   
   The site controller is the ‘off the line’ control application managing all administrative tasks. It is providing interfaces to ERP and/or MES systems for exchanging order, batch and serialization related data; alternatively it can be configured to operate as a full standalone master data management application. The PharmaSuite based site controller is connected to a DB server for storing mass data; furthermore, order related serialization data management as well as randomization, serial ranges, reporting functionality and aggregation visualization is located here. Performing rework activities like de-aggregation and re-aggregation using mobile devices completes the off-line functionality of the site controller.

2. **Line Controller**
   
   The line controller is the bridge between the automation layer and the level 3 world. It is exchanging data with the site controller while at the same time managing and synchronizing the connected line aggregates via a Rockwell Automation PLC. The communication to the machine PLC is handled via standardized interfaces using PackML¹ thus supporting also connection to non-Rockwell Automation components.

3. **Machine HMI and Device Control**
   
   The individual machines of the complete lines are receiving their specific serial ranges from the line controller and transfer back the real serialization data created at machine level. The machine control is providing a HMI and the respective device controls.

Rockwell Automation is uniquely positioned to provide a comprehensive serialization solution.

¹PackML: industry standard for machine communication
Rockwell Automation’s Integrated Architecture provides a fully integrated and scalable solution.

- The automation layer to control the discrete and motion related Serialization functions. The Logix control platform provides this functionality using a single development environment and a single, open communication protocol. Thus Rockwell Automation’s Ethernet/IP protocol allows real time processing and, by realizing the serialization at PLC level, error sources compared to PC solutions – like power supply units and CPU’s – are eliminated.

- The information layer to configure, manage and store serialization information with the FactoryTalk Production and Performance Suite. On a line level, across the site and even across the enterprise. Thanks to Rockwell Automation’s Ethernet/IP protocol, connecting various lines is a kind of build in functionality and requires no additional efforts.

Rockwell Automation’s Global Services capabilities ensure a low risk implementation of all aspects of the serialization solution, starting with serialization assessment studies, specification and realization of the solution. Rockwell Automation’s tremendous domain knowledge ensures also the support of the complete validation cycle.
A common use case for a serialization solution could be described as follows. As a part of a complete packaging line, folding boxes get packaged into cases and finally put onto pallets.

### Serialization – A typical use case

The serialization solution is charged with tracking which item went in what. The basic flow is similar for all item levels:

- Print a unique barcode (or write RFID info) onto the item
- Verify the content with a camera (or RFID reader)
- Eject the item in case of any inconsistency

Multiple potential line setups are possible. In a nutshell, the challenges on a line level are always to be able to identify the aggregation structure, verify the quality of printed barcodes and trigger ejection in case of failures.

Those challenges especially occur when applying retrofit solutions to existing and validated packaging lines. There is no out of the box approach that could be applied to all packaging lines. In particular for tracking bundles an individual line assessment has to be made to evaluate the most feasible solution approach and the most secure process. Thanks to Rockwell Automation’s broad industry experience supported by its large OEM network we can provide the best qualified personnel performing such assessments.

### Serialization – Plant level features

At the plant level manufacturers need to provide the capability to prepare the lines for serialization as well as to store product serialization and aggregation information as generated by the shop floor manufacturing. The amount of data to be handled is massive. The Rockwell Automation solution provides the following capabilities:

- Coverage of all relevant IT layers from ERP via MES down to the automation layer.
- Serialization module can either be integrated in a level 3 system architecture or be used stand alone.
- Interface capabilities to MES and/or ERP systems to automatically transfer context data of packaging runs like product name, product number, batch number and expiry date.
- Interface capabilities to MES, ERP or specific Serialization systems to automatically
transfer serialization details like starting sequence number, list of sequence numbers and ranges of sequence number in the case of using randomized, non-sequential numbers. Data is exchanged in an EPCIS² conform format.

- Randomization capabilities that produce randomized sequence numbers in a given number range. The used algorithm, named “Mersenne Twister” is a very robust and proven algorithm which is common in the clinical supply area to blind clinical studies.

- Data transfer to OEE component via interface.

- Built in aggregation module for flexible definition and handling of hierarchy levels of level 2 system items.

- Active directory integration promotes the use of the same user credentials as in other shop floor systems.

- Data storage for high data volumes

- Archiving capabilities

- XML- Reporting for creation of serialization records

- Plant engineers use line setup and device configuration parameters adapting the behavior of the serialization shop floor solution to the physical parameters of the packaging line.

- The operator uses electronically controlled work instructions to manually interact with the system. The solution supports use cases like test runs. A smaller amount of packages will be produced by the line. Afterwards the operator verifies if the applied barcodes of the packaged goods are in line with the expected result. With that, the line setup can be verified upfront.

Other use cases like the manual re-entering of packages in the line helps to control complex re-packing process in the case of a failure.

Sampling functionality supports the activities of quality assurance (QA).

All manual interactions are documented by an audit trail.

- Easy connection of lines allowing multi-line control thanks to Rockwell Automation’s Ethernet/IP protocol technology, which is also guaranteeing real time processing in a high speed environment.

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² EPCIS: Electronic Product Code Information Services (interface definition for exchanging product data)
**Serialization – Shop floor automation features**

At the automation level the solution provides the following advantages and capabilities:

- Add-on equipment to existing lines (retrofit solution)
- PackML based pre built libraries for OEMs for connecting Rockwell Automation components across level 2 and external devices like cameras and printers.
- Printing and monitoring of the barcode printer
- High speed communication to the scanner / vision inspection systems
- Reading and analyzing of the scanner / vision inspection results
- Creation of the aggregation information
- Controlling of the ejection mechanism
- I/O connections

In summary, the line controller in conjunction with the machine automation layer controls the printing, verification and rejection of the barcodes applied to the units and documents the physical results. The scalable controller based architecture allows a real-time environment, which is the foundation to meet current and future performance requirements. Add-on capabilities to existing lines ensure to minimize interruption of production and minimize the validation burden.

Direct high speed communication via Rockwell Automation’s Ethernet/IP protocol minimizes data traffic and therefore avoids data transfer bottlenecks even though dealing with huge data amounts. Shifting the solution to a scalable PLC architecture minimizes technical error sources and allows real time processing in a high speed environment as well as guaranteeing a highly available solution over multiple lines.
Serialization – Equipment and device integration

Rockwell Automation’s integrated architecture concept offers easy and flexible integration of hardware components like printers, cameras and RFID components needed in the Serialization context.

High speed printers for printing the data matrix code onto the products and special cameras for performing the vision inspection are the key components of a serialization system.

RFID can be used instead of or in addition to the data matrix barcode for supply chain optimization or for fulfilling special industry needs. For an overview of Rockwell Automation’s RFID capabilities please visit http://www.rockwellautomation.com/solutions/.rfid/

Rockwell Automation has a long time experience by implementing high speed printing, RFID and vision inspection solutions. Leading companies in the Food, Pharma and Clinical Supply area are printing with our solutions (e.g. printing of patient labels with 2D barcodes using “Wolke” printers and performing vision inspection control afterwards).

Rockwell Automation has a variety of partners as well as a large OEM network providing the respective expertise in the context of high speed printing, RFID and vision inspection systems and retrofit solutions.

The close partnership with leading companies led to preferred integration capabilities of Rockwell Automation’s controller architecture with the above components. That means less integration effort and less risk of implementation.

CIP – Communication Industrial Protocol – networks (with EtherNet/IP for Serialization) are used by all Rockwell Automation components thus simplifying design, start-up and maintenance and reducing costs throughout your plant with common control and communication services.

By using products such as the EtherNet/IP to DeviceNet Linking Devices, all device network segments can be easily tied together using an EtherNet/IP backbone. The seamless bridging and routing capability of CIP networks ensures that all devices can communicate to each other regardless of which network they are on. In other words, one controller and one programming
terminal is all that you need to control and configure all the devices. This significantly simplifies
the system architecture allowing better manageability and easier maintenance.

This technology also offers highest availability and is capable of handling huge data amounts in a
high speed environment.

**Solution Focus**

Rockwell Automation develops technologies and provides services that leading manufacturers
around the world use to their competitive advantage. Whether running a single machine or an
entire supply chain, manufacturers rely on their automation, power control, and conversion
products and services to manage information flow from plant to plant, from plant floor to front
office and from country to country to get their products and services to market faster, to reduce
costs, to better utilize power and plant-floor assets, and to minimize risks in their manufacturing
environments.

**Customer Support and Maintenance**

Manufacturers today are looking for ways to maximize productivity, solve problems or satisfy a
need while managing costs. Maintenance provides one of the last remaining areas of the plant to
realize significant impact on both financial and production metrics such as:

- Increased production rate
- Elimination of unplanned downtime
- Decreased scrap or waste
- Improved financial stability
- Reduced maintenance costs

Rockwell Automation’s Strategic approach to maintenance blends an appropriate mix of
predictive; preventive and reactive maintenance strategies that will help meet production and
business goals.

For additional information on Rockwell Automation Services & Support, please visit:
http://www.rockwellautomation.com/services.

**Serialization – Summary**

Drug counterfeiting is a serious threat to the public health. Countermeasures need to be globally
coordinated. There is no silver bullet to address all challenges at once. One element for the
success of the fight against drug counterfeiting will be the capability of the industry to come up
with innovative solutions to track material seamlessly from the manufacturer to the consumer.

Technological implementations for Serialization are the technical basis for providing crucial supply
chain security. Rockwell Automation, as the leading company for automation and information
solutions can assist in fighting the battle against drug counterfeiting.

Rockwell Automation provides the right solution approach thanks to its

- Complete solution approach covering all areas of serialization across an enterprise,
- Technological expertise in the automation business and the advantages of its automation
  layer design,
- Strong experience in the Life Science industry especially related to interfacing to various
  systems in an existing IT landscape.