Watch more

Australia

Meeting regulatory requirements through the use of GS1 standards

Challenge

Several countries now require serial numbers to be present on pharmaceutical products, and for this data to be transferred from the manufacturer to the regulator. In 2017, the pharmaceutical company Aspen Australia was awarded a significant contract manufacturing portfolio, with many of the resulting products being exported to nations in which such requirements were in place. The company therefore needed to implement a solution to ensure compliance.

Approach

Aspen Australia implemented a multi-level serialisation solution. The implementation has successfully enabled Aspen Australia to supply a significant volume of serialised product to the numerous export markets, fully compliant with countries' regulatory requirements. The use of GS1 DataMatrix and EPCIS standards has been central to this. The system has been deliberately designed such that it can be built upon in the future to meet further regulatory requirements.

A need to ensure serial numbers are present on products in several different markets

Requirement for serial number data to be transferred to the market authorisation holder

Full compliance with all current relevant regulations

Ability to expand the system for future regulatory requirements

Introduction

The regulatory requirements related to pharmaceuticals have been constantly evolving over the past decade, with an increased focus on the detection of falsified medicines and the traceability of prescription medicines. To ensure the integrity of the pharmaceutical supply chain, improve the safety of medicines and combat counterfeits, the European Union (EU) developed the Falsified Medicines Directive (FMD). This outlines the requirements for printing unique identifiers (serial numbers) on pharmaceutical products and the transfer of the associated data from the manufacturer to the regulator. Several other overseas markets have implemented similar guidelines, intending to provide a system that can verify the authenticity of pharmaceutical products at the point of sale.

In 2017, Aspen Australia was awarded a significant contract manufacturing portfolio. This was to be implemented over the ensuing five-year period, with the commercialisation of products staged between 2018 and 2021. Of this new contract manufacturing volume, a large portion would be exported to Middle Eastern markets (including UAE, Bahrain, Jordan, Oman, Lebanon, Kuwait, Qatar and Saudi Arabia). When added to Aspen's existing contract export volumes (which included products for South Korea and the UK) it was forecast that the Aspen facility in Dandenong (a suburb of Melbourne) would need to supply more than 11 million sales units per annum into markets that had regulatory requirements for serialised products. The common thread for all target markets was the use of a GS1 compliant DataMatrix barcode for the encoding of machine-readable unique identifiers onto pharmaceutical packs.

To meet the anti-counterfeiting requirements of the FMD and equivalent requirements issued by Middle Eastern and South Korean market regulators, in late 2018 the Aspen Dandenong site embarked on the journey towards implementing a serialisation system, to enable the contract

manufacture of products sold into these markets. The upfront challenges Aspen faced were:

- Commencing the serialisation project with a very low local knowledge base.
- Sourcing of equipment and solutions that did not exist in Australia and/or had not been implemented in Australia.
- Timing of solution implementation, to tie in with the target commercialisation dates of large-scale manufactured export volume and various in-market mandatory serialisation deadlines.
- Performing sufficient due diligence around the solutions to be implemented, knowing that such systems would become embedded in how Aspen operates and hence would be difficult to change further down the track.
- Implementing solutions that could be expanded to incorporate future packaging requirements, regulatory requirements and scope of serialisation (such as aggregation/track and trace).

Developing understanding and specifications

Before attempting to specify and source a serialisation solution for the Aspen Dandenong site, members of the project implementation team needed to perform some initial research to gain an understanding, even at a very high conceptual level, of how a serialisation system typically works.

This included reaching out to Aspen's internal global network and to the contract customers for which the company would produce and sell serialised products. As much information as possible was gathered about the software and equipment solutions they had implemented, system hierarchy and workflow drawings, system specification documents and operating procedures.

This research was supplemented by information received from both serialisation system solution providers and market regulators. The regulatory documents released by the EU to support the FMD (Commission Delegated Regulation (EU) 2016/161) are well-written, easily accessible documents that describe how unique identifiers shall be printed onto packs. They also provide a theoretical overview of the serial number lifecycle, and of the flow and management of associated data from manufacturer to regulator through to point of sale. This, as intended, enables the verification of the authenticity of pharmaceutical products.

The scope of Aspen's implementation was limited to Point of Dispense Authentication (PoDA – see Figure 1), which means that serialisation was only required at the sales unit packaging level. This is a subset of full track and trace (which involves identification and movement of

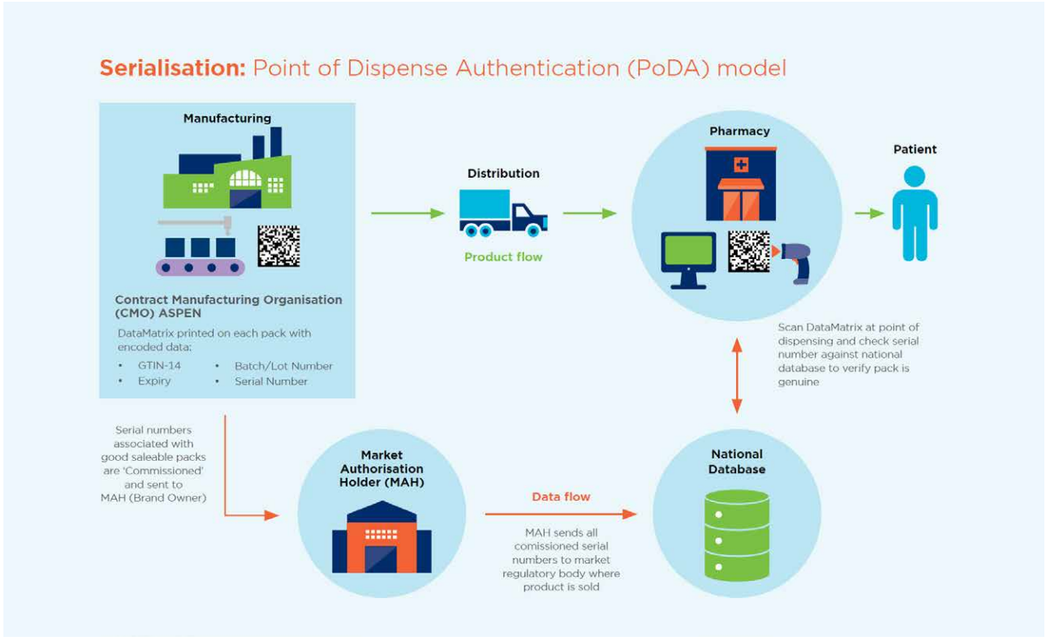


Figure 1

The implementation

Aspen implemented a traditional serialisation model of **Level 4**, **Level 3** and **Level 2** systems (Refer to Figure 2).

Aspen Serialisation System Infrastructure

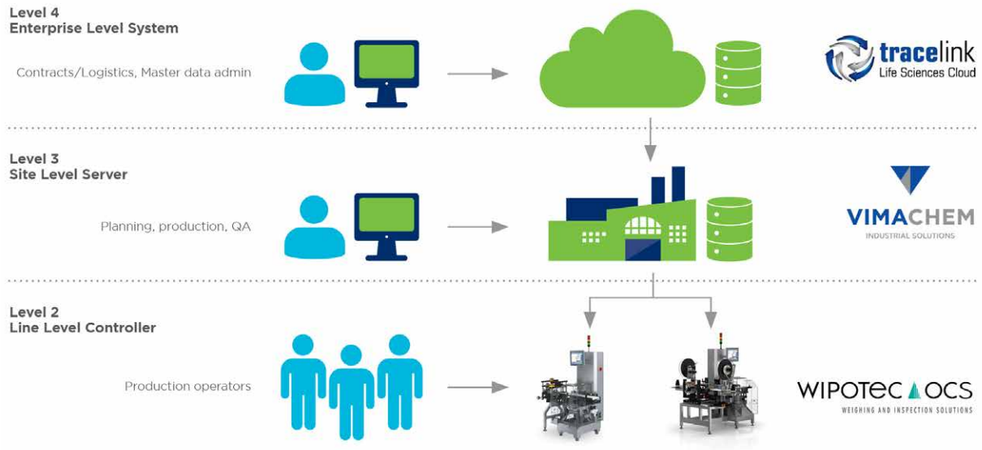


Figure 2

data through the supply chain) and of aggregation (in which there is a requirement to serialise at all levels of packaging). Given that various markets are heading towards requiring one or both of these, it was crucial that any solution implemented by Aspen could be built upon in future to achieve such requirements.

The following selection criteria were therefore formalised for the tender process:

- **Flexibility:** The ability for system layers to integrate with alternate third-party equipment and/or software solutions in the future (ie. universal interface) instead of 'locked in' proprietary systems.
- **Scalability:** The ability to expand the system, both through the addition of more packing lines and increased functionality on existing packing lines (eg. shipper- and pallet-level aggregation).
- **Ease of use:** User interfaces that were as simple and logical as possible.
- **Balance of ubiquity and innovation:** Striking a balance between well-proven system solutions and finding opportunities to embrace new technology based on lessons from other serialisation implementations.
- **Implementation and validation support:** A resource for validation protocol generation, technical implementation, and validation execution.
- **Customer service:** Ongoing technical support post-implementation, via service level agreements or otherwise.
- **Cost** was also a key consideration of course; both the capital implementation cost as well as any continuing or volume-based fees for the likes of software subscriptions, service level agreements or commissioned serial numbers.

The solution and its implementation

Aspen implemented three distinct levels of infrastructure, which follow the traditional serialisation model and are referred to as Level 4, Level 3 and Level 2 serialisation systems (See Figure 2.)

The enterprise level system (Level 4) is the 'brains' of the serialisation system:

- Contains all company, partner and product master data.
- Manages serial number pools per product, which are either internally generated or externally replenished (depending on the customer's preference) and with quality controls to ensure uniqueness.
- Has a business to business (B2B) interface with Aspen's contract customers for transacting serialisation data.
- Is a data repository of all serial numbers transacted to meet regulatory obligations.

Aspen selected the cloud based TraceLink application as the enterprise level system. It was primarily selected for its wide and established network of B2B connections linking many pharmaceutical companies, including all of Aspen's contract customers. In addition, TraceLink's regular automated internal validation programme ensures monthly software patch updates do not impact the validated state of the application interface. This means Aspen receives a service where much of the complexity of maintaining the system is outsourced.

The implementation was led by a small project team from TraceLink. Considerable input was required from Aspen's internal and external stakeholders in understanding and agreeing on the business workflow they were trying to achieve. The team had to configure the system master data accordingly (first in a test environment, and subsequently in a production environment) and then test the connections between the Aspen site and the company's contract partners.

Site and line level systems

The site level server system (Level 3) is used for batch management at a single manufacturing facility. It is in this system that serialised orders are created, assigned to lines, monitored for status and finally quality released. This is the software layer most frequently accessed by day-to-day technical operations, meaning that the system needed to have a clean, user-friendly interface. It also needed to be able to support a range of access levels, corresponding to the types of users that interact with the system.

Aspen selected Vimachem Site Serialisation Manager (SSM), following a review of several proposals and software demonstrations from different vendors. Vimachem SSM was deemed to be best aligned with Aspen's selection criteria. It is also designed to seamlessly integrate with TraceLink and has a universal (non-proprietary) interface with the line level serialisation equipment.

The implementation was led by a small project team from Vimachem. Members of the team remotely managed the application connections at the required stages of the project, developed all specification documents, and executed a validation package across both test and production environments.

The line level controller system (Level 2) serialisation equipment is at the 'coal face' of serialisation. It receives the serial numbers from the higher-level software systems, undertakes the printing of the DataMatrix and human readable text onto packs, verifies the data and the barcode quality, performs other ancillary functions (such as the application of tamper evident labels and check weighing), accepts/rejects packs, and commissions or deactivates the corresponding serial numbers.

As Aspen's initial serialisation launch was across five packaging lines, the Level 2 system implementation would take up a majority of the project budget and present the highest level of risk to timeline, functionality and future flexibility if not chosen correctly. Aspen therefore initiated a large tender to eight different vendors of serialisation equipment.

Wipotec OCS (Germany) provided the best overall fit to meet Aspen's selection criteria and was selected to supply all the Level 2 systems. The company offered a highly integrated solution with relatively simple setup and operational procedures and have a universal (non-proprietary) interface for future flexibility. The Wipotec OCS line level controllers can also be extended upon with additional systems if full aggregation is required.

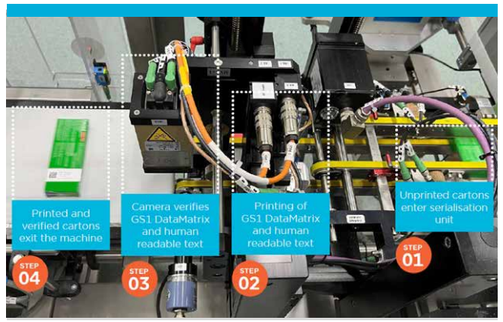
The implementation of each Wipotec OCS serialisation unit included a Factory Acceptance Test (FAT) in Germany and subsequent installation, qualification and Site Acceptance Testing (SAT) on Aspen's premises by a Wipotec OCS technician, and/or by technicians from the local machine agency.

The workflow and process

- As a contract manufacturing organisation, Aspen's serialisation workflow begins with the automatic replenishment of product-specific serial number pools in the enterprise level system (TraceLink), with serial numbers externally sourced from the market authorisation holder's enterprise level system.
- When a serialised order is created in Aspen's site level server system (Vimachem SSM), the required quantity of serial numbers is request-

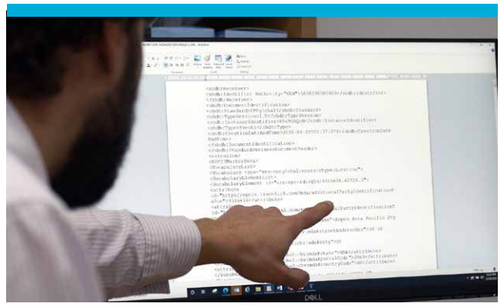
ed and downloaded from the TraceLink number pool. These serial numbers are removed from the available pool and move to a 'Reserved' state in TraceLink.

- When the order is due to be packed, a user in Vimachem SSM will assign the order to the corresponding line level controller system (Wipotec OCS) and the serial numbers for this order will be downloaded onto the unit.
- Each pack processed by the Wipotec OCS unit will be assigned a unique serial number from the order. The machine will print a unique GS1 DataMatrix barcode encoded with the GTIN-14, expiry date, batch/lot number and serial number and will inspect it by taking a photo of the barcode and human-readable text elements. Acceptable packs are classified as 'OK' and are allowed to continue on the production line. Packs that are not acceptable are classified as 'NOK' and will be automatically rejected and quarantined.



- For every pack processed, various pieces of information are linked to each corresponding serial number in the order data. This includes the OK/NOK status, expiry date, batch/lot number, date/time of processing, GS1 DataMatrix read quality, the reason for rejection (if NOK) and pack weight (for lines with an integrated check weigher).

- After the order is packed, it is ended on the Wipotec OCS unit and the order data (including the disposition of all serial numbers as accepted, rejected or unused) is updated in Vimachem SSM.
- The order data remains in the site level server system pending quality release. During the final stage of quality release, a QA user will approve the commissioning of the order in Vimachem SSM to allow the transfer of the completed order data to the enterprise level system (TraceLink).
- All serial numbers in the TraceLink repository associated with the order (which up until this point have remained in a 'Reserved' status) are updated with their final disposition. The serial numbers associated with good saleable packs are commissioned and the lot-specific information (captured by the lower-level systems) is now linked to these serial numbers in the database. The serial numbers associated with rejected packs are deactivated and can no longer be used. Any residual unused serial numbers from the order are returned to the available number pool and their status is changed back to unreserved.
- Coinciding with the physical shipment of stock from Aspen's premises, a shipment transfer is performed in TraceLink. This sends the serialisation data for all commissioned packs to the market authorisation holder, together with Global Location Numbers (GLNs) describing the source and destination of the physical goods. This transaction is contained within an Electronic Product Code Information Services (EPCIS) XML file which is a GS1 standard for sharing event data and updating entries in external database systems.



- This is the final stage of the serialisation process for Aspen as the contract manufacturing organisation. The market authorisation holder will report the commissioned serial numbers to the regulatory database of the target market in which the goods are to be sold. This provides a means of verifying the authenticity of pharmaceutical products at the point of sale.

The challenges

It took Aspen two years from conception to go live of the serialisation system (August 2018 to July 2020). The first nine months were research, pre-tender and tender phases before the final solutions were nominated. During the project, the biggest implementation challenge faced was, unsurprisingly, the validation effort involved in implementing and launching three layers of networked infrastructure, (cloud-based, Aspen server-based and factory floor-based) to meet pharmaceutical regulatory standards.

The single most valuable document to be generated during the project was therefore the project validation plan. This set out the validation strategy as a roadmap of the various implementation milestones, across the three layers of infrastructure and in both test and production environments, culminating in performance qualification exercises to rigorously test the system end-to-end.

Lessons learned

For organisations looking to start their serialisation journey, the key advice from Aspen is:

- Invest adequate resourcing into the validation process
- Allow time for stakeholder management. This is extensive and may be across several time zones, requiring strong project management and flexibility to work non-standard hours to align with overseas support
- Provide dedicated resourcing for the generation of standard operating procedures and operating manuals, as the serialisation system will introduce several new business processes across various departments
- Allow sufficient time for user training and embedding of the new workflows. This will be a very new and different way of working for many staff but Aspen's experience is that it will soon become the new normal.

"It was fortunate for Aspen that the ten different target markets adopted a standardised method for encoding the unique serial number and other critical information onto their packaging, and that method was the GS1 DataMatrix. Furthermore, the means of sharing serialisation event data between us (the Contract Manufacturing Organisation) and all our customers (the Market Authorisation Holders) is via an Electronic Product Code Information Services file (or EPCIS file for short) which is also a global GS1 standard. Hence what made this complex project more manageable and allowed us to implement a single 'catch-all' solution was the widespread adoption of GS1 standards."

Michael Hadjion,
Engineering Manager, Aspen Australia

Next steps

In addition to the five serialised packing lines implemented during the initial project, Aspen is currently in the process of adding three more serialised lines over the next 12 months. This is primarily to increase the flexibility of their solid dose blister packing operation by unlocking capacity for more packing lines to meet the growing demand for export (serialised) products from the facility.

Conclusion

Two years have passed since the commercial launch of the serialisation system (July 2020). The implementation has successfully enabled Aspen Australia to supply a significant volume of serialised product to numerous export markets, fully compliant with the countries' regulatory requirements through the use of GS1 DataMatrix and EPCIS standards.

About the author

Michael Hadjion
Engineering Manager Aspen Australia

Michael Hadjion is engineering manager at the Aspen Australia manufacturing facility located in Dandenong South, Melbourne. With 18 years of experience in the pharmaceutical industry, he initially specialised in equipment and facilities validation before heading into project engineering and maintenance roles. Joining Aspen as project manager in 2012, Michael has delivered a diverse range of projects including major capital works, contract manufacturing tender submissions, and the transfer of a large portfolio of consumer and over the counter products into the Aspen facility. Between 2018 and 2020, Michael managed Aspen Australia's serialisation system implementation.

About the organisation

Aspen Australia is a wholly owned subsidiary of Aspen Pharmacare Holdings Limited (South Africa). Commencing operations in 2001, the firm is now one of the largest pharmaceutical companies in Australia and has one of the most comprehensive portfolios of medicines in the country. This includes prescription pharmaceutical brands, generics, specialty products, over the counter (OTC), and consumer healthcare products.

Aspen Australia operates a single large-scale manufacturing facility located in South Dandenong, Melbourne. In addition to the manufacture of Aspen branded pharmaceuticals, the Dandenong site has a rapidly expanding contract manufacturing and export business.

www.aspenpharma.com.au

About GS1 Healthcare

GS1 Healthcare is a neutral and open community bringing together all related healthcare stakeholders to lead the successful development and implementation of global GS1 standards, enhancing patient safety, and operational and supply chain efficiencies.

The development and implementation of GS1 standards is led by the experts who use them: pharmaceutical and medical device manufacturers, wholesalers, distributors, group purchasing organisations, hospitals, pharmacies, logistics providers, solution providers, governmental and regulatory bodies, and trade associations. Evidence available from industry implementations shows that GS1 identification, data capture and data sharing standards in healthcare deliver tangible benefits to all stakeholders. Global members of GS1 Healthcare members include more than 115 leading healthcare organisations worldwide.

Follow us on **social media**

Linkedin.com/showcase/gs1healthcare
Twitter.com/GS1healthcare
Youtube.com/GS1healthcare

Visit our **website** and the **Reference Book digital portal**

www.gs1.org/healthcare
www.gs1.org/industries/healthcare/reference-book-portal

(01) 0 9504000 32301 1

GS1 Global Office
Blue Tower, Avenue Louise 326, bte 10, Brussels, B-1050, Belgium
T +32 2 788 78 00 | **E** info@gs1.org
www.gs1.org