Optimizing Delivery of Global Pharmaceutical Packaging Solutions, Using Systems Engineering Patterns

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Abstract. The global pharmaceutical supply chain, a complex system, involves manufacturing, distribution, and commercial wholesale/retail processes. Products in this system-of-systems are critical to health, subject to regulation from a web of trans-national, national, and state/provincial authorities, and subject to commercial manufacturing, marketing, and distribution practices of numerous enterprises. Introductions of change into this environment is a challenging undertaking, demanding awareness of the many forms of and constraints upon this system, while delivering at the brisk rate required by law and commerce. For example, in response to drug counterfeiting and grey markets, national and local governments are currently introducing (differing) legal requirements to uniquely label and track pharmaceutical products to the individual retail bottle/package level, as they move through distribution. This paper describes the response of a global pharmaceutical manufacturer, re-engineering multiple global product and country-unique pharmaceutical product packaging lines, using Systems Engineering Patterns to reduce impacts of variable requirement and design configurations.

The Global Pharmaceutical Distribution System

The Overall Distribution System. The overall distribution system for pharmaceuticals can be quite long and convoluted. Manufacturers often produce products for world wide distribution in multiple countries. Products move from the manufacturing site to the manufacturer's distribution centers, then to the wholesaler's central and then regional distribution centers, and then to the retailer's distribution centers and ultimately to the retail pharmacies or hospitals. In some cases, the product is also repackaged for a different market, adding complexity. This is the simple view of the distribution system; often wholesalers or retailers also sell to each other and move product back and forth from country to country. The entire chain may be configured differently in different enterprises and countries, and for different products.

Packaging Lines. Many Pharmaceutical companies have packaging lines in multiple sites around the world. Each line is configured to produce a certain range of products. One line may package many products, but it is unlikely that any one line would be capable of producing the full range of products produced by a manufacturer. Some sites or lines are only approved to provide products to certain markets depending on what regulatory approvals that particular line has been granted. Some sites may package thousands of unique products, some differing by their literature inserts and package labelling. Managing the number of lines, the capabilities and capacities of each line and the markets that line is approved for can be a complex problem. This is often a discipline or function within pharmaceutical companies.

Many pharmaceutical companies make use of contract manufacturing to leverage their own capabilities and capacities. This further complicates the problem of managing the supply chain.

Related Information Systems. Serialization of product label information is an information intensive undertaking:

1. Information systems coordinate the allocation of unique label identifiers to individual units within manufacturing lots, requiring coordination of enterprise-level information systems with real time production floor control systems;
2. Information systems consume and make available the outcome of individual product unit labelling, providing that information to downstream distribution customers (wholesale, retail, and consumer) who potentially need to be able to correlate it with what they find on the labelled product they receive.

The systems involved in package serialization thus combine enterprise, and real time information systems with packaging and labelling equipment, production procedures, plus distribution transport and storage. The equipment and information systems across the globe are often not of standardized vendor or configuration.

Packaging Serialization—
An Example of Complex System Evolution

Hypothet Pharmaceuticals has packaging operations in 10 countries serving 160 different markets. With all of their different products and presentations (strengths, sizes, counts) there are 5000 different SKUs. There are 100 packaging lines. Not all packaging lines are able to serve all products or markets. Additionally Hypothet Pharmaceuticals has agreements with 3 Contract Manufacturers with locations in 6 countries serving 80 markets.

Drivers for New Laws and Regulations. There are some current and emerging legislation happening world wide to require unique identification of saleable pharmaceutical products. There are two drivers for this legislation:

1. Counterfeit medicines are becoming a problem for patients. Per the WHO (World Health Organization) Website: “Counterfeiting is greatest in regions where regulatory and enforcement systems for medicines are weakest. In most industrialized countries with effective regulatory systems and market control (i.e. Australia, Canada, Japan, New Zealand, most of the European Union and the United States of America), incidence of counterfeit medicines is extremely low – less than 1% of market value according to the estimates of the countries concerned. But in many African countries, and in parts of Asia, Latin America, and countries in transition, a much higher percentage of the medicines on sale may be counterfeit.”
2. In countries where there is reimbursement for medications, fraud is becoming a problem. Requests for reimbursement may be made for counterfeit or non-existent medication.

The current and proposed legislation (which itself a dynamically changing system, calling for agile systems engineering capabilities) takes two general forms:

1. A scheme in which a unique serial number is assigned to a item of sale and then tracked through the entire supply chain from the manufacturer to the patient with a mechanism for being able to detect through electronic records where legitimate products have passed from owner to owner, and where counterfeit materials entered the supply chain. Since most saleable products are small enough that they are packaged in cases and then on pallets, the cases and subsequently the pallets must then uniquely identified and the item, case, and pallet data must be associated so that the chain of custody can be established. This scheme provides an electronic path to follow in the event that counterfeit products have been sold into the legitimate supply chain. This scheme is generally known as "Track and Trace".
2. A scheme in which only the item of sale is uniquely serialized and it checked for the correct serial number at the point of sale or point of reimbursement. This scheme is generally known as "Authentication".

Additional Related Applications. If item level products are uniquely serialized, this data may be able to be used with other business processes such as complaint investigation, product recalls, marketing and others. This is a further source for stakeholder needs and system requirements.

Considerations. The regulations in each market are developing, with some markets favoring the "Track and Trace Scheme" and some markets favoring the "Authentication" scheme. The effective date of these regulations is shifting with some approved legislation being pushed back, and some pending legislation appearing to be moving up.

An enterprise would not want to waste capital on modifying packaging lines with "Track and Trace" capabilities for markets that will not adopt the "Track and Trace" scheme since that would be spending resources for value. Nor does it want to add the capability to rush provide "Authentication" capability to lines before the hospitals, and pharmacies have the ability check the unique serial number since this would be spending capital and disturbing operations prior to the serial number on the package actually being useful to the patient.

Two problems face the enterprise:

1. Understanding the technical issues around serializing saleable items for both the "Track and Trace" and "Authentication" schemes well enough to develop or purchase a technical solution that can be applied within the regulatory timelines.
2. Understanding the delivery process to implement the technical solution across the breadth of lines and locations.

A Systems Engineering View of the Problem

The Requirements and Design Variability Challenge. For all the reasons cited above, it is important that a global Packaging Serialization design solution (1) accommodate unique local needs essential to specific legal and regulatory authorities and product lines, while (2) preserving as much common content as possible across the globe to maximize enterprise leverage. This is the "variable sameness" challenge that is commonly found in managing product lines, platforms, and configurable enterprise systems that must, in different market sectors, locations, or applications, at the same time be "the same" and "different"—both of these for good business reasons.

Common design solution content begins with common system requirements—two different countries' solutions need to at least share some common requirements if they are to share some common design content. Figure 1 illustrates the related idea of a "pattern" of common system requirements, configurable to the needs of specific locations or product lines:

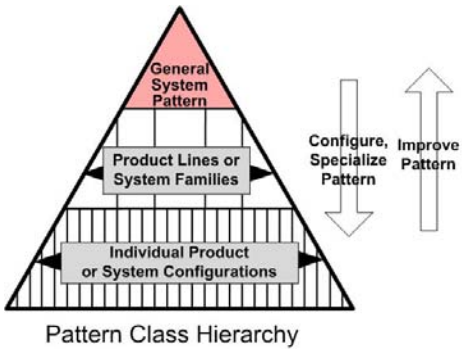

Figure 1: One System Pattern, Configurable for Different Sites and Applications

The Delivery System Challenge. The business processes required to deliver, install, and qualify changes to pharmaceutical product packaging lines are themselves complex systems. Individual country sites represent differences in business practices, local support contractors, and other related processes. Executing all these across numerous global sites at a brisk commercial pace requires an understanding of the delivery process as a configurable system in its own right.

In this global program, Lilly treated both the delivered packaging line system and its delivery (engineering, installation, qualification) process as equally important formally modeled systems. Just as the core Packaging Serialization Pattern is configured to describe the requirements and design of the packaging solution for each site, so also is the Packaging Serialization Delivery Process configured to describe how delivery is to proceed at each site—including installation, qualification, training, and turn-over.

Applying Systems Engineering Patterns

Configurable Model-Based Requirements and Designs. Lilly developed its specific configurable patterns of packaging systems and their delivery systems using the general Pattern-Based Systems Engineering (PBSE) methods described in more detail in (Schindel and Smith, 2002; Schindel, 2005b). By configuring such patterns for the needs of a specific site, a set of Model-Based requirements are rapidly generated that describe the unique needs of a site project.

The "Model" created by this process is an explicit data structure (Schindel, 2005a; INCOSE, 2009) that includes multiple model components:

- System Domain Model (system boundaries, diagram, actors, external interfaces, etc.)
- Stakeholder Feature Model (stakeholders, features, attributes)
- System State Model (states, transitions, events)
- System Interaction Model (functional interactions, functional roles, attributes)
- System Requirements Statements
- Physical Architecture (physical components, relationships, attributes)

- Other Model components as needed (e.g., failure modes, verification methods, etc.)

A Pharma Manufacturer's Use of PBSE. Lilly has applied Pattern-Based Systems Engineering (PBSE) to create a family of configurable Systems Engineering Patterns for various pharma manufacturing applications—one of which is packaging serialization. While the Lilly-specific patterns are considered proprietary company intellectual property (IP) assets, the general methodology is more widely applied, and illustrated by the following simplified examples:

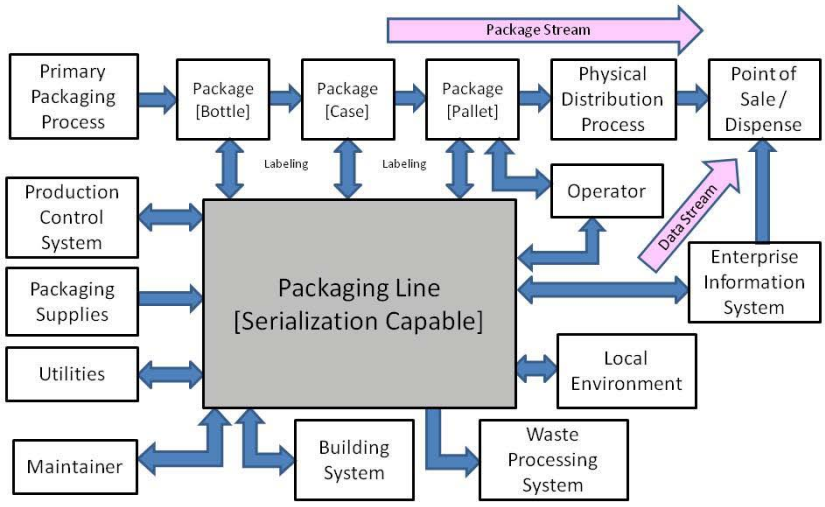

Figure 2: Configurable Domain Model of Serialization Packaging Line [Simplified]

- Feature: Package Serialization—The feature of generating labelled packages with unique serial number label data and matching information system records, in support of fraud reduction and other applications.
- State: Line Running—The operational state in which the packaging line is applying serialization data to packages.
- Interaction: Apply Package Label Data—The interaction of the packaging line with packages, during which label data is applied to the packages.
- Requirement: "The system shall apply package label data as indicated by the [Label Data Parameter and Format Table] to the package, at a line rate of up to [Max Packaging Line Rate]."

Our Approach

Constructing Patterns. We have constructed a configurable, re-usable Packaging Serialization Pattern describing the requirements and design of packaging line serialization systems, configurable for different global sites and products. The investment of effort to construct this

configurable pattern was on the same order of magnitude as the effort projected to specify a single packaging line, but we obtained a re-usable asset. This also helps leverage a global procurement process that might otherwise be addressed one purchased solution per line at a time, and increases options to leverage global suppliers.

Configuring Patterns. Pattern-based methods explicitly differentiate between the construction and improvement of the Pattern versus the configuration of the Pattern for specific sites or jobs. The configurability of the Pattern (for example, selection of the applicable package hierarchy and setting the packaging line speed) makes explicit what aspects may be changed during the configuration process and what aspects remain fixed across different configurations. This means that traditional systems engineering "trades" can in many cases be built into the Pattern in advance of its configured uses. For example, rules about manual, semi-automatic, and fully automatic package inspection options can be considered in advance and built into the Pattern with configuration rules that indicate when each of these different configurations may be optimal.

Validating and Applying Patterns. We validated the Packaging Serialization Pattern by using it to describe the requirements and design of a reconfigurable captive test packaging line, and subjecting the result to review by company engineers as well as packaging system suppliers. The pattern was used to generate a set of system requirements used as the basis for an RFP against which bidders wrote proposals, as the basis for purchase contracts, and as the basis for acceptance test generation. Requirements were found to be more complete than might have typically been expected for a complex system without using these systems engineering techniques.

Additional Work. Work is now underway in using this configurable pattern as the basis for a global delivery process that is addressing multiple packaging sites.

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BIOGRAPHY

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William D. Schindel is president of ICTT System Sciences, a systems engineering company, and developer of the Systematica™ Methodology for model and pattern-based systems engineering. His 40-year engineering career began in mil/aero systems with IBM Federal Systems, Owego, NY, included service as a faculty member of Rose-Hulman Institute of Technology, and founding of three commercial systems-based enterprises. He has consulted on improvement of engineering processes within automotive, medical/health care, manufacturing, telecommunications, aerospace, and consumer products businesses. Schindel earned the BS and MS in Mathematics, and was awarded the Hon. D.Eng by Rose-Hulman Institute of Technology for his systems engineering work.