White Paper

Achieving Regulatory Operational Excellence

Unified Quality and Regulatory Information Management

A Ennov White Paper
website: http://ennov.com

Content

Introduction

Budgetary pressures, expiring patents, smaller R&D pipelines and an evolving regulatory landscape are just some of the challenges currently facing the life sciences industry. These challenges are causing many companies to reevaluate their current business models in order to compete more effectively in existing markets and fuel new growth into emerging markets. Simply put, it is no longer business as usual. Many life sciences companies are looking for new ways to achieve their business objectives more effectively and efficiently. As they try to reshape themselves they are reducing costs, streamlining processes and striving to become leaner and more innovative entities.

An important part of this transformation is the thorough examination of key Regulatory processes that are critical to getting a product to market quickly and keeping it there. Moreover, the processes that span organizational boundaries are especially significant as they are often made more complex by disconnected IT systems and compartmentalized operating procedures. One process that is particularly important is the process of managing variation submissions – mostly due to their time sensitivity and regulatory impact. This whitepaper examines the variation submission process, identifies areas of risk and opportunities to mitigate those risks through unified Quality and Regulatory Information Management.

Managing Variation Submissions

The efficient management of variation submissions can be challenging. While these submissions are vital to keeping approved products on the market, the essential processes and technologies to effectively manage them are often overlooked.

The work required to fully implement a manufacturing change and create its accompanying variation submission is typically performed by different departments within a company – Manufacturing, Quality Assurance (QA), Supply Chain and Regulatory Affairs. Often, each team completes their work separately with little or no visibility into the activities being performed by the other teams.

To make matters worse, the teams may lack a comprehensive understanding of the overall variation process and how their work impacts that of the other departments and the company as a whole. In addition, the outsourcing of some or all of the process can further complicate the situation.

This combination has the potential of introducing the risk of a product non-compliance. To mitigate this risk, many companies have initiated efforts to harmonize processes and standardize the interactions between contributing teams with the intent of increasing efficiency, improving communication and eliminating

bottlenecks. The result of these initiatives are typically a catalogue of process maps, RACI matrices and standard operating procedures (SOPs) each intended to build consensus among stakeholders, recognize breakage points and identify areas for improvement.

Let's consider a very basic process map to illustrate the organizational and technological interdependencies associated with a variation change control and submission.

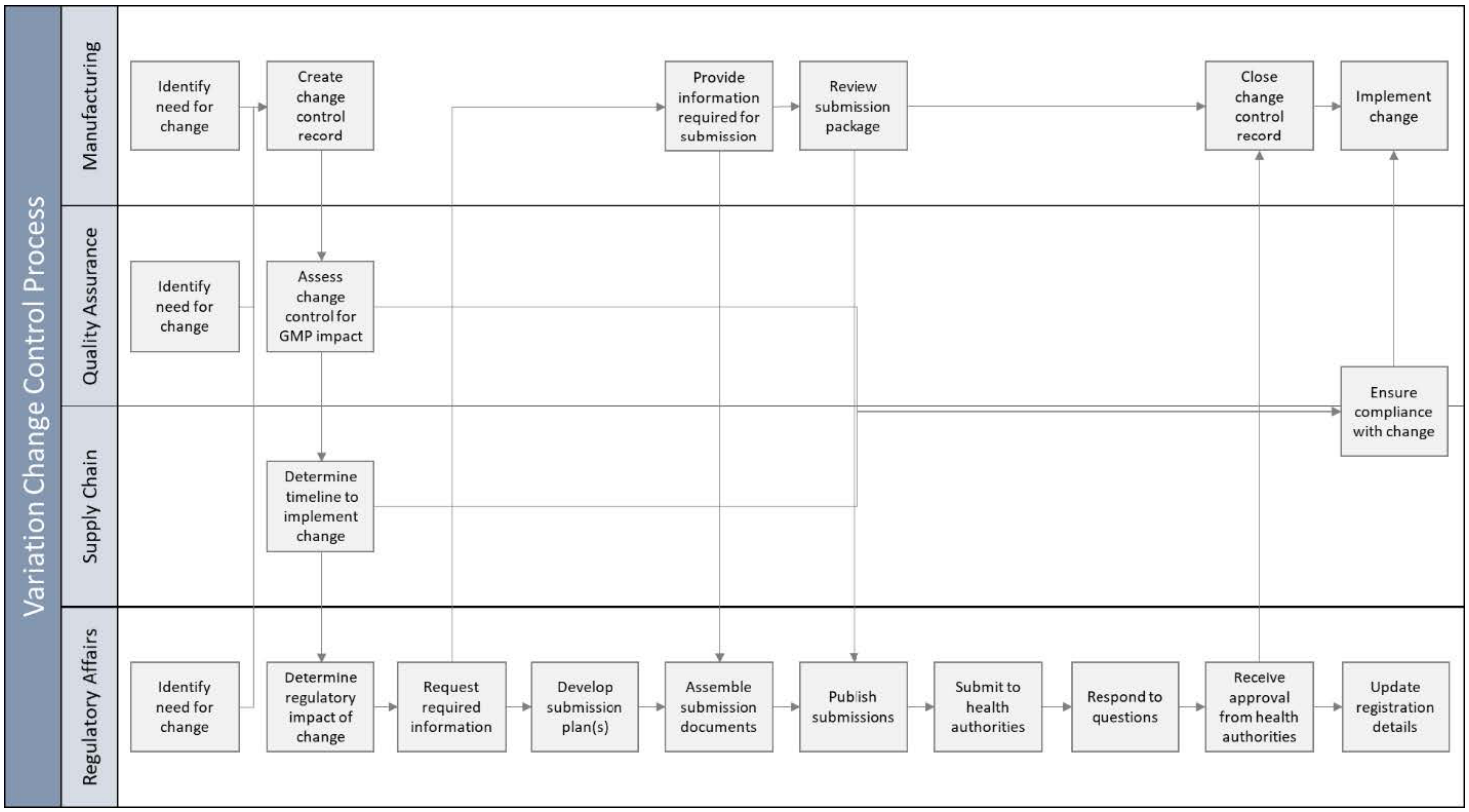

Figure 1 – Variation Change Control Process Map

The process map plainly shows each team's responsibilities and the required interactions between them – answering all of the "what" questions.

The verbs "create", "assess", "request" and "develop" are clear calls to action and the swim lanes establish accountability for each step in the process. The linear progression of the process steps implies answers to the "when" questions but provides little or no guidance on specific activity timings, lead-times or durations.

What is missing from this recipe altogether are the answers to the "how" questions. For example, when Regulatory Affairs requests information from Manufacturing to support the submission is this done through email, by telephone or using some other means? When Manufacturing reviews the submission package prior to dispatch to the health authority is it performed on paper or electronically?

Finally, how is Manufacturing informed of health authority approval so the change can be implemented without delay? Now, more than ever before, companies are relying on enterprise information systems to help them answer these "how" questions – relying on each system's functionality to enforce compliance with their processes and procedures.

However, systems that are disconnected or loosely integrated can actually complicate matters, adding unnecessary overhead, introducing compliance risk and making it more difficult to meet the aggressive timelines required to prepare and publish compliant regulatory submissions.

Understanding the Systems Involved

Fundamentally there are five enterprise systems involved in the management of the variation change control process:

- Enterprise Resource Planning (ERP): Manages and tracks raw materials, active ingredients and finished products. Facilitates production planning throughout the manufacturing process. Provides visibility into stock levels to ensure order fulfillment and on-time delivery. Ensures quality control requirements and regulatory compliance obligations are met at all times.

- Quality Management System (QMS): Automates, centralizes and consolidates the capture, tracking, management and regulatory reporting for all quality processes and practices. Common processes include the management of deviations, non-conformances, complaints, audits, change controls, and CAPAs.

- Electronic Document Management System (eDMS): Manages the lifecycle of digital content files (documents, spreadsheets, images, etc.) from initial creation through archiving. Provides version control, facilitates review and approval cycles and manages distribution. Regulates access to content files through rights management, provides metadata-based and full text searching capabilities.

- Regulatory Information Management Systems (RIM): Manages and tracks medicinal product details and registration information. Product details include API, manufacturing, packaging, distribution, composition and stability information. Plans and tracks regulatory submission projects and related activities. Manages correspondence and commitments between the sponsor and health authorities.

- Electronic Publishing System (EPS): Builds regulatory submission structures, publishes and validates compliant submissions in a variety of output formats (CTD, eCTD, NeeS, VNeeS, eCopy and paper). Provides bookmarking and hyperlinking to improve navigation. Accesses and links regulatory content from eDMS or file system.

In many instances these systems operate independently from one another – each serving the unique needs of their users. However, much of the information that is managed within each system is common to all of them.

The most obvious example of this is the Active Pharmaceutical Ingredient (API). To illustrate the impact of this data redundancy, let's consider the case of changing an API manufacturing site. The API is directly linked to the packaged product SKUs managed in the ERP, to the change control record managed in the QMS, to the API manufacturer documents in the eDMS, to the submission sequence for the variation in the EPS system and to the product registration information in the RIM system.

Changing the manufacturing site in the ERP system triggers a cascade of updates that must be made in each of the remaining four systems to maintain compliance. If this process is manual, it must be well coordinated and controlled.

System Interaction: Data and Processes

To further appreciate the scope of the data and process dependencies between these systems consider the following diagram:

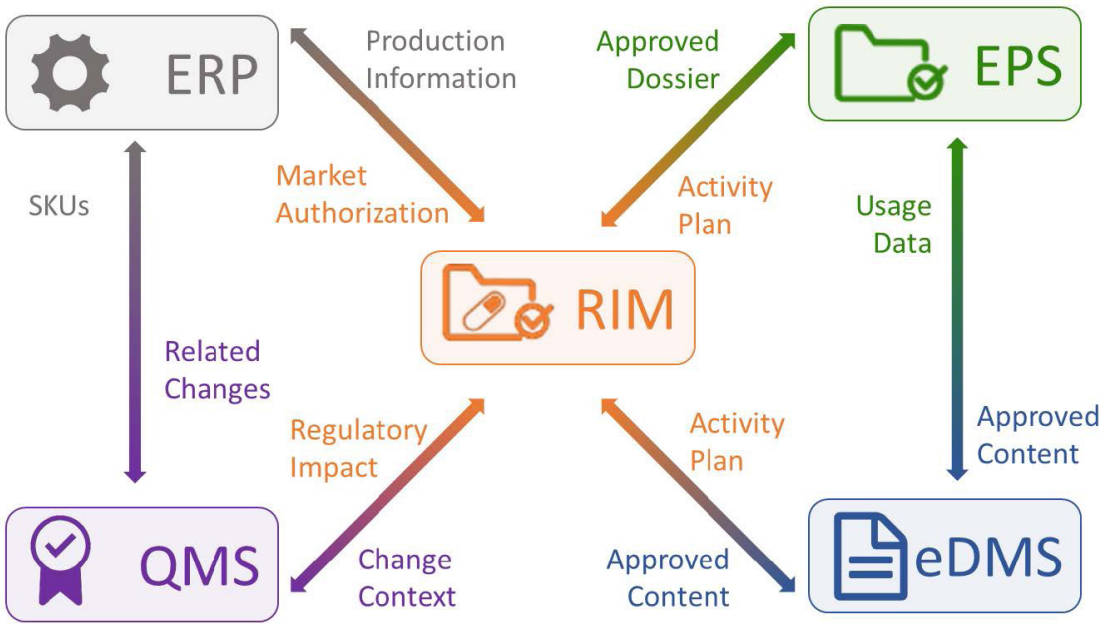

Figure 2 – Data and Process Dependencies

The end-to-end variation change control process requires linkages between the systems to either directly access data (e.g. packaged product SKUs, serialization information) or reference data (e.g. approved submission documents and dossiers). In the worst case, there are no links and references to this information are managed manually. This is done by re-keying referenced record IDs or URLs into the other systems or maintaining a list in departmental spreadsheets. These practices, because they rely completely on human action, are inefficient and error prone which introduces non-compliance risk.

Another way to address the issue are automated links between the systems. Automated links eliminate the need for human intervention and increase the reliability of the referenced data.

Automated links can be implemented in one of two ways – interfaces or integrations. Interfaces are lightweight links that simply share information between the systems. This information could be a common key such as a marketing authorization number that links to a particular SKU or a change control number that links to a series of variation submissions. Examples of these shared fields are further illustrated in the following diagram:

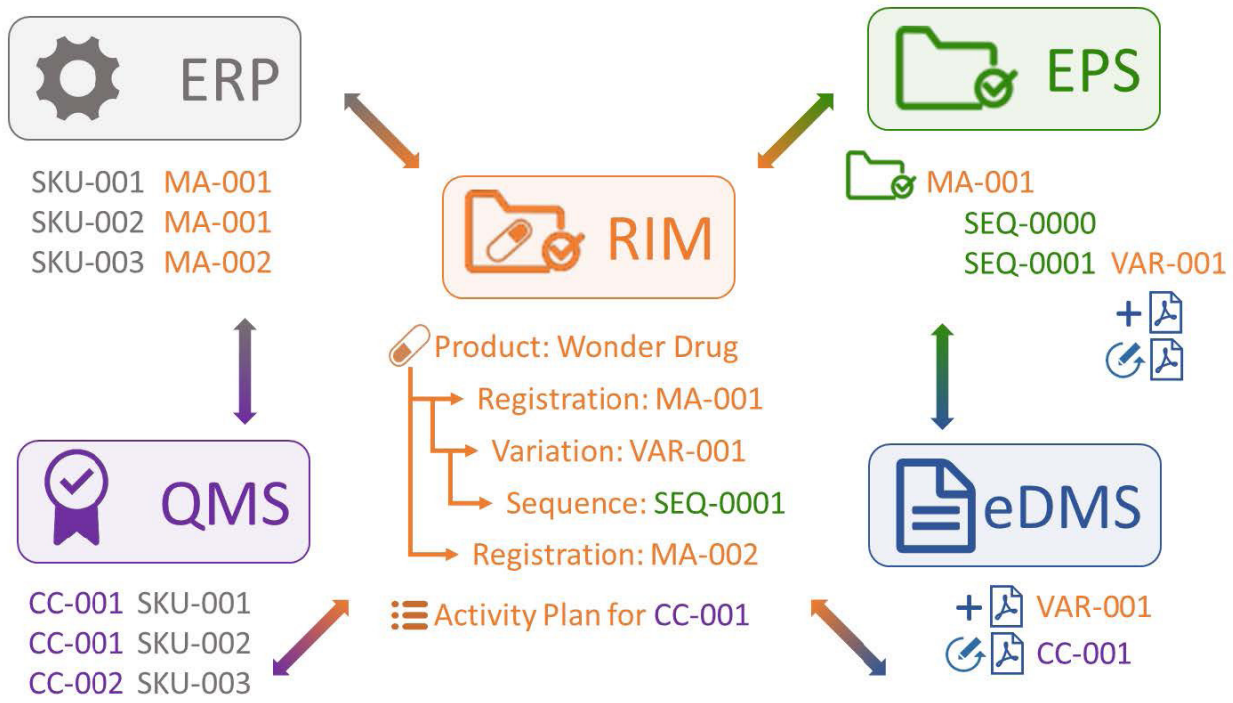

Figure 3 - Shared Data Fields

With a system interface, only data is shared – which does little to ensure the "how" questions are being answered consistently. A more robust approach to system linkage is system integration which includes both shared processes as well as shared data.
In the example above, a system integration could cause the RIM system to notify the ERP system which SKUs are authorized for production once regulatory approval is received. In the case of a change control, the QMS could trigger a process within RIM to initiate a regulatory assessment of the change and its impact on the specific SKUs covered by the marketing authorizations in each country or region. Activity plans for the affected registrations could be created and workflow notifications sent to the Regulatory CMC and Publishing teams requesting new or updated documentation and new eCTD submission sequences.

System integration removes process variability – which is the key to mitigating compliance risk. However, system integration can be quite complex, difficult to maintain and expensive. Often, the systems (particularly the older legacy ones) have different architectures that make integrating with them nearly impossible. Updates to one system can have an adverse effect on the integrations with the others, requiring extensive testing and re-validation. Integrations that were not well designed and have evolved over time are particularly dangerous. In many cases, the original designs were not well documented or the design documentation has not kept up with the evolution of the integration. This confluence of circumstances often leads companies into a state of "system paralysis" where their manual processes must be maintained in order to compensate for the limitations of their legacy enterprise systems.

A Better Way: The Unified Platform

Imagine a solution where all of the information required to effectively manage the variation process is available from a single authoritative source.

A solution where regulatory data, documents, dossiers and the process workflows to manage those assets are intrinsically linked together – facilitating seamless operation and efficient communication across departments.

A solution where everyone references the same controlled vocabularies and where regulatory changes are implemented for everyone, globally, at the same time.

A solution where closing the loop on a change control once final regulatory approval is received becomes automatic and where information from across the value chain can be leveraged to improve organizational performance and achieve operational excellence.

To some, this solution sounds unrealistic and will be dismissed straight away. To others, this solution sounds intriguing and warrants a closer look. And finally, to others still, this solution sounds very familiar because it is what they use every day to achieve world-class status with respect to unified Quality and Regulatory Information Management.

In order to understand the concept of the unified platform, it is important to understand what it is not. The unified platform is not simply a collection of purpose built applications (or modules) that are integrated through a series of pre-built connectors. It is, instead, a highly configurable software architecture that combines a common and engaging user experience (UX) with business process management, document management, data/forms management and business intelligence to form the foundation on which all unified applications are constructed.

As a result, all applications are natively connected and do not require custom integrations to facilitate interoperability. A common, harmonized and configurable data model eliminates redundancy and ensures data accuracy and consistency across all applications. Custom interfaces to link related records together become immaterial as all information is inherent to all unified applications.

Because all applications involved in managing the process share a common UX, users can focus on completing their assigned work and not on mastering the nuances of multiple specialized systems. Common activities such as navigation, searching, item creation and task acquisition are performed identically – regardless of context.

Cross-organizational communications and collaboration are enhanced, process and information silos are eliminated and the “how” questions are answered consistently. Total transparency into regulatory processes is achieved – eliminating bottlenecks while ensuring timelines are met and commitments fulfilled.

This unified and ubiquitous approach to human-computer interaction results in higher user adoption rates, lower training requirements and overall increased productivity. Finally, the unified platform reduces the overall cost of compliance through the reduction of annual software support and maintenance fees, faster employee ramp-up and lower re-validation costs following system upgrades.

The following figure illustrates the concept of the unified Quality and Regulatory Information Management solution. The users can seamlessly navigate the information hierarchy from the initial change control, through the regulatory activity plan and product information and to the effected documents and related regulatory submission dossiers.

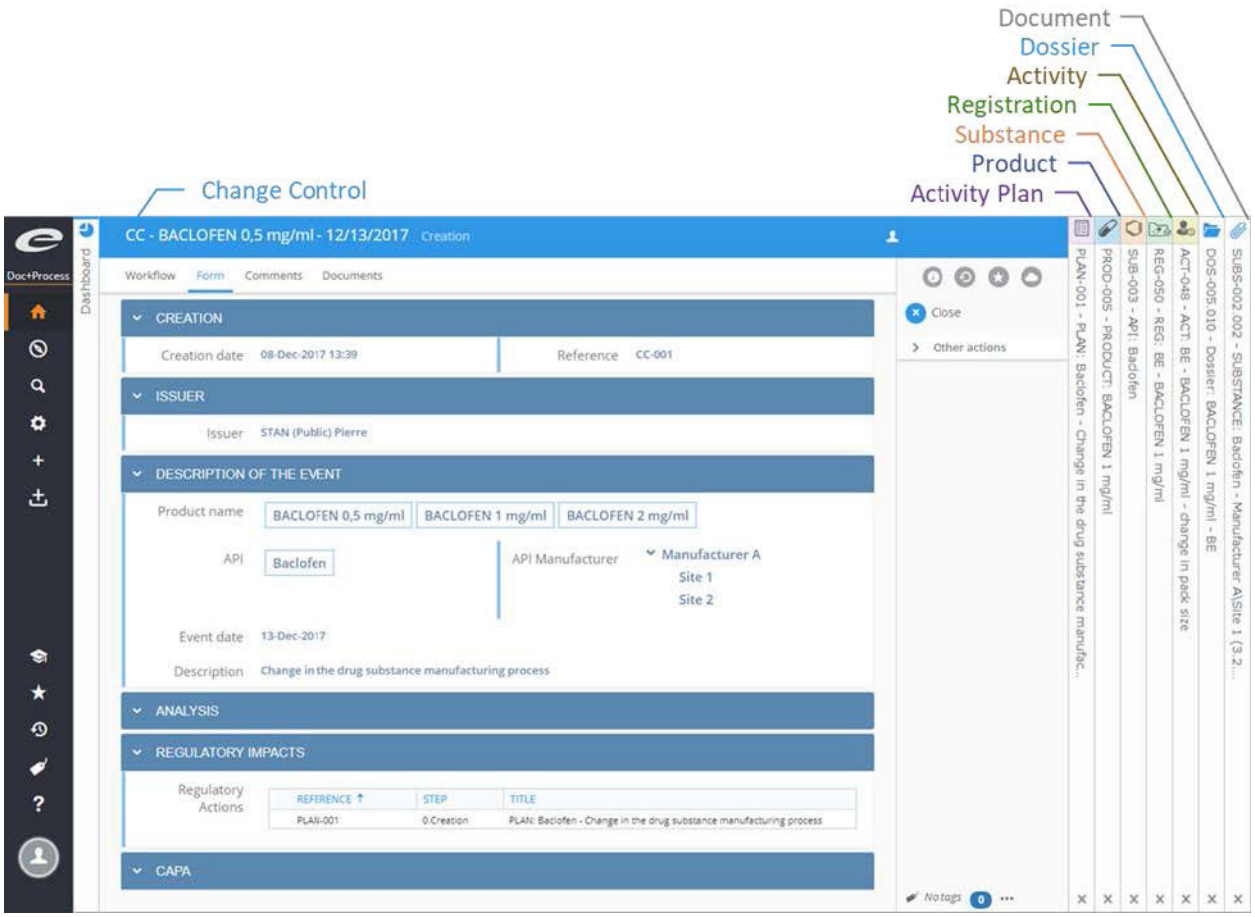

Figure 4 - Unified Quality and Regulatory Information Management

Summary

It is clear that a variety of challenges facing life sciences industry are causing companies to examine high-value operational processes (such as variation change controls) in an effort to become leaner, more efficient and remain competitive.

Process harmonization and standardization programs can only take a company as far as the IT systems being used to support them. Disconnected or loosely-connected enterprise systems require human intervention to share data between them – a practice that is error prone and introduces compliance risks. Bespoke system interfaces and system integrations are expensive, complex and do not come without their own set of issues – most notably system upgrade paths and forward compatibility concerns. The unified platform is, by definition, an intrinsically connected software framework on which a set of applications used to manage regulated content, data and processes is built. This end-to-end, holistic solution eliminates the risk associated with customized integration points, improves user satisfaction and reduces the total cost of compliance.