The use of process mapping in regulatory affairs

Authors

Corinne Gaulton, *Consultant, Real Regulatory Limited, UK & Ireland;* ***Lucy Herlihy,*** *Senior Consultant, Real Regulatory Limited, UK & Ireland.*

Keywords

Process map; Variations; Compliance; Manufacturing; Quality assurance (QA); Quality control (QC); Quality by design (QbD); Change control; Supply chain.

Abstract

Process mapping – the creation of a diagram or "map" to identify all the steps and decisions in a process – has become a hot topic in regulatory affairs. Such mapping allows the monitoring of regulatory processes by providing greater visibility of each step of the process; it indicates the responsibilities and interactions between departments, and leads to better communication and understanding. It can also help identify inefficiencies and thus result in improvements to procedures and reduce overall costs.

This article discusses process mapping for use in regulatory submissions, specifically addressing the challenges of variation submissions, and provides the basics for creating a process map.

Challenges of variation submissions

There are a number of challenges involved in trying to ensure regulatory submissions are made in a timely and efficient manner. Similarly, there are inherent challenges in trying to ensure that changes which require regulatory submissions are recognised at an early stage, are addressed appropriately and are a reasonable use of resources.

The work undertaken to maintain a product on the market by each of the departments within a company is sometimes done in relative isolation, with no team having sufficient visibility or appreciation of the work of other teams or the impact this has on the overall output of the company. This situation poses a serious risk for product compliance.

To mitigate this risk, an ability to liaise closely and map clearly the key interactions of each department within a company is critical to ensuring regulatory compliance. In particular, the interaction between the manufacturing and regulatory affairs functions is essential for efficient management of changes. In the absence of well-defined processes and interactions, the manufacturing team may omit to alert the regulatory affairs team in sufficient time of potential changes, leading to delays in submissions and issues with stock control. In addition, the manufacturing function may not be aware of the regulatory impact of minor changes and may not appreciate the need to consult the regulatory affairs function to assess this, resulting in lack of compliance of the manufacturing process with the registered information. The impact from a regulatory perspective can be substantial, requiring a great deal of work and potentially a series of consecutive regulatory submissions to be filed under significant time pressure to achieve timely compliance.

With the emergence of new ways of working, the interaction between the two functions becomes even more closely interlinked. For example if a quality by design (QbD) approach is applied, manufacturing process changes within the defined design space will not require submission of a variation. Central to the success of the QbD approach is the need for a robust change control procedure that clearly maps out any process changes and determines the impact of the changes to the manufacturing process. Therefore, effective cross-functional communication and team work across multiple departments is critical to the introduction and overall understanding of the QbD concept.

It is imperative that feedback from the quality assurance (QA) department is sought by both manufacturing and regulatory affairs departments when any change is planned to the manufacturing process. Similarly, audit findings by QA need to be evaluated by the manufacturing and regulatory affairs teams in order to assess the impact on the manufacturing process and any potential regulatory impact. Thus QA is often seen as providing the link between manufacturing and regulatory affairs departments. If this link is not strong enough, QA will not have sufficient oversight of the process to overcome the very specific QA challenges of ensuring that all changes are in compliance with good manufacturing practice (GMP), that the product is consistently produced in compliance with the registered information and that all batch information and records are within specification, transparent and sufficiently documented.

It is vital for the supply chain team to be aware of the projected timelines for achieving approval of a variation. This information dictates the management of logistical operations, ensuring that supply of a regulatory-compliant medicinal product in a particular market is synchronised with patient demand and that the obligation of the marketing authorisation holder (MAH) to ensure continuity of supply in the market is fulfilled.

In the past, the manufacturing department was the driver of the supply chain – managing the pace at which products were manufactured and distributed. Increasingly, the importance of strategic input from the regulatory affairs team and the value of timely submissions and approvals are being recognised as one of the key drivers of ensuring supply of a medicine meets patient requirements in all markets.

Insufficient interaction between the regulatory affairs and supply chain teams, coupled with inadequate submissions can lead to rejections or delayed approvals which can, in turn, result in out-of-stock

situations. This can have regulatory implications and can also impact on patients. In addition, from an economic perspective, minimising the amount of old stock following approvals of variations is an important issue which can be addressed by efficient planning and understanding of the process. The process needs to incorporate sufficient flexibility to cater for these eventualities. To effectively plan production and supply to markets, approval dates need to be accurately projected by the regulatory affairs department and communicated effectively to the supply chain team. It is also essential to have a defined process in place to ensure all stakeholders are informed if there are any delays to the approval process so that the risk of an interruption of supply to the marketplace is minimised.

Benefits of process mapping in variation submissions

It is all too often the case that unnecessary errors are made while planning regulatory submissions. They may be a result of a lack of communication between departments or of particular departments not knowing where they "fit" in the variations procedure. It is important that people know exactly when they will be required to get involved in the process and how they ultimately affect the outcome.

Process mapping creates and improves the culture of collaborative working with greater awareness among the individual teams of how their element of the overall work fits into the wider picture. There is an increased integration of departments with other business operations such as manufacturing, analytical development, supply chain, etc, impacted by proposed changes.

A successful process map improves the quality management system and increases traceability of the process with clearly defined responsibilities and timelines (which can be added to the process map). Process mapping is also beneficial to new clients, new staff and local regulatory affairs offices. Their roles and the departments with which they cooperate are easily and visually explained. All members from each department are made aware of the process mapping exercise and by contributing to this, they can identify and rectify any deficiencies. Where an efficient operation exists, there can be some margin on timeframes, so that flexibility can be factored in for unexpected eventualities without creating unnecessary pressure on deadlines.

A streamlined procedure

Preparing for a variation submission is a time-consuming and complex process, with the dual challenges of tight submission deadlines and the preparation of compliant documents. Reference to a process map provides clarity to all departments on the evidence required to satisfy regulatory requirements, and minimises the risks of repetitive mistakes and duplication of effort. The regulatory submission becomes a streamlined process involving clearly defined activities and interactions from the planning stage to submission of the variation (and post submission). This leads to faster approval and implementation times, increased competitiveness and increased productivity. Meanwhile, the quality control (QC) and QA teams benefit from greater cross-functional support and communication, ensuring that both quality and compliance are at the forefront of each department's objectives. In addition, the risk of an out-of-stock situation developing is significantly reduced and the chances of "old stock" having to be destroyed are minimised. The process map will also identify the weakest points in the process and bring focus to these as areas for improvement.

How to create a process map

There are four major steps involved in process mapping:

1. Identifying the process to be mapped and the objectives for mapping
2. Collecting information – interviewing key users and stakeholders and brainstorming to create the map
3. Creating the map from collected information
4. Reviewing the map with users and stakeholders to gain agreement on the process and to make improvements to increase efficiency.

It is obviously important to involve key users and stakeholders in the process mapping exercise, as they will be best placed to describe the steps that they are involved in. A team comprising representatives from all departments who have a good overview of the process should be involved in creating the process map. A member of the team who drives the discussion should have some knowledge of the process mapping technique. The boundaries of the process should be decided along with the process start and end. The process map can either show enough information to understand the general process or detail every action and decision.

At the beginning of the exercise, the steps of process need to be identified, starting at the trigger for the process. All steps should include a verb to start the task description. The four main symbols to be used in a process map are triggers for the start and end, decision and documents. If the process being mapped becomes too complex it is possible to extract some steps to create sub-processes on separate maps. The team should be allowed to follow the process from start to finish and decide on one outcome for each decision. To cover all eventualities, it is advisable to go back to work out every outcome from each decision. Post-it notes can be useful during a brainstorming session to allow tasks to be moved within the process. Once all steps are decided, responsibilities and/or "swim lanes" (where each activity is assigned a "lane", visually demarcating responsibilities for specific process steps) should be added. It is also possible to insert timelines in the process map to give an indication of expected timings of each step.

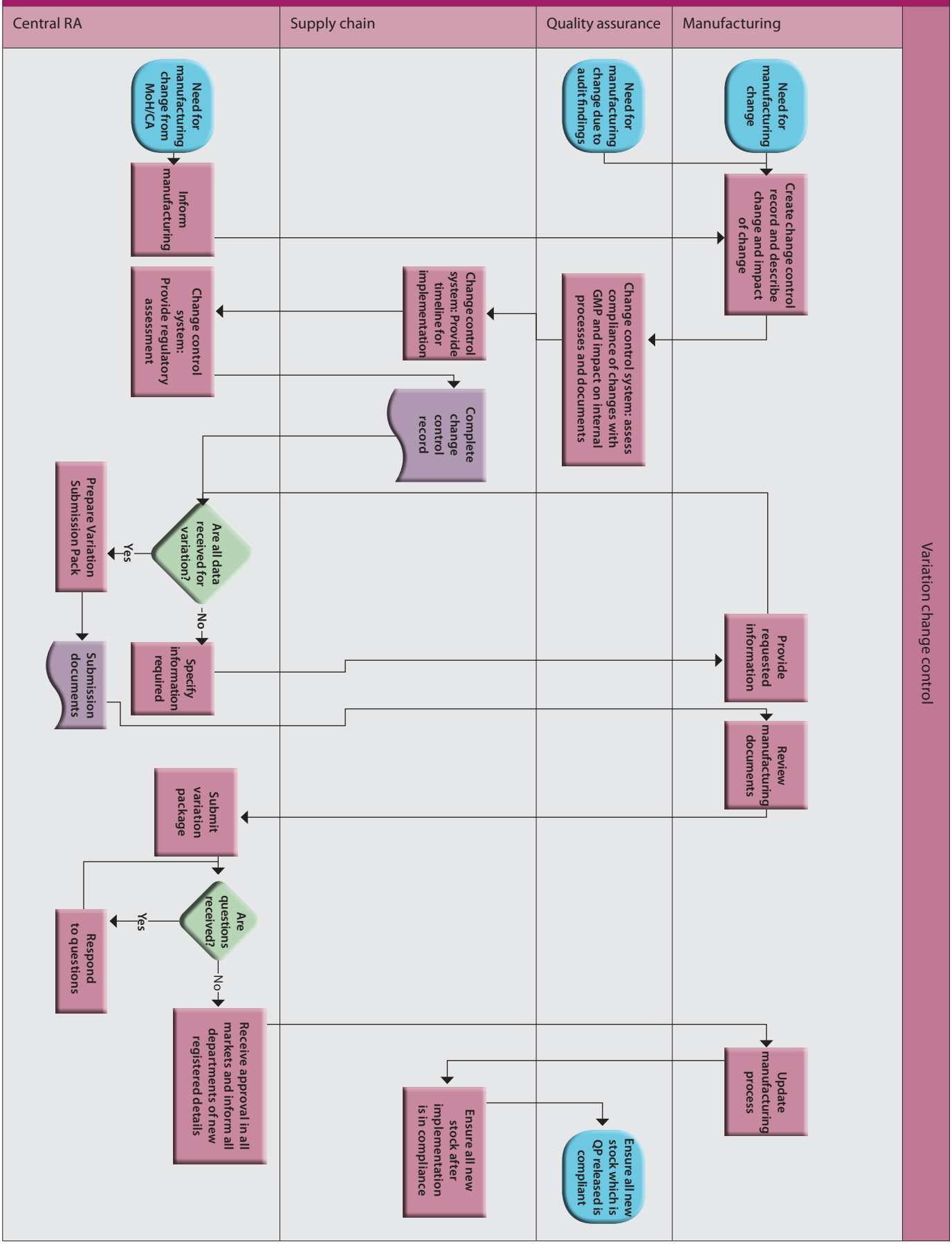
The initial process map should be kept as simple as possible. The map should then be sent to key users and stakeholders for review, allowing for discussion on any missing elements or redundant steps. At this stage, analysis can also be conducted to eliminate any existing waste or inefficiencies in the process, following which final agreement on the process map can be reached. It is important to remember that the process map should be kept under regular review (reviewed at least annually) to take into account changes such as company restructuring and changes in legislation or best practice.

Uses of process mapping in regulatory affairs

The process map in Figure 1 shows a simplified process map for preparation, submission and approval of a variation, depicting the multiple responsibilities for each function involved in the process. Other uses for process mapping within regulatory affairs include:

- Document management: Multiple inputs and review cycles for documents can make version control and efficiency difficult. Different functions need to understand their responsibilities for document preparation, and all those involved need to be aware of the timelines and the rate-limiting steps in this process. Document preparation across multiple functions is often rate-limiting in regulatory submissions, and delays at this stage can directly impact submission timelines.
- Submission of a clinical trial application showing preparation of all individual documents such as the investigational medicinal product dossier (IMPD) and investigator's brochure (IB).

Figure 1: A process map for variation change control.



- Preparation and submission of a marketing authorisation application.
- Overall clinical drug development – a process map can represent the drug development template for a company.
- Individual large regulatory projects, eg, grouped Type II variation. For larger regulatory projects it may be beneficial to have a process mapping meeting before the start of the project to ensure all departments are aware of the steps and timelines for the individual project.
- Responses to questions and queries from agencies need to be submitted in a timely manner and can affect the schedules of manufacturing and QC departments if additional information is required. A process map can define the interaction between stakeholders and help clarify at which point queries may arise in the submission process.

Process mapping can also be used in internal procedure preparation, for example:

- Internal standard operating procedures (SOPs): Written SOPs can often result in overly complex procedures to be followed. Preparing a process map within a team before SOP generation can ensure the whole team has input into the procedure, which should result in increased compliance. In this way a process map can be the starting point for preparing written procedures. These process maps can be incorporated into the written procedures to allow users to visualise the process. SOPs and other procedures based on clearly defined processes are generally more simple and straightforward and are easier to follow. A process mapping exercise can also be conducted during revision of written procedures to ensure the procedure matches the process and is as efficient as possible.
- ISO 9001:2008 standards, which aim to provide beneficial quality management systems, focus on a process approach as opposed to procedures. Following this approach of process mapping to clearly define internal processes before procedures can ensure the company processes are accurately represented in an improved quality management system.

Conclusion

Process maps are a valuable tool for any company facing regulatory and economic challenges. From a regulatory perspective, process maps can improve the efficiency of the submission procedure through proper planning. Visualisation of a process can assist in identifying each department's role in the process and who their decisions are likely to impact. It can improve submission and approval times, thereby eliminating either out-of-stock or old stock situations.

Process mapping helps streamline strategic planning of variations by involving all stakeholders of the process. If the need for submissions is identified early on in the process, decisions can be made more quickly and the time pressures and cost for regulatory affairs departments can be reduced. Unnecessary errors in planning variations and in their submissions due to inefficiencies and lack of awareness between departments can be reduced. Process mapping as part of the regulatory process can be a reliable and constant feature in an ever-changing regulatory environment. Visual processes which are easy to understand are generally well worth the time and effort it takes to create them.