Total Project Management Solutions for Development of Veterinary Medicinal Products

PEER REVIEWED

Development, Scale-up, Validation and Marketing Authorisation

The introduction of new pharmaceutical veterinary products is dependent on a wide range of activities, through development and manufacturing to clinical field trials and building the regulatory dossier. This requires the support of multiple teams working in a coordinated approach.

A key activity, and the focus of this article, is the transfer of the process development knowledge into a cGMP manufacturing facility (likely to be a contract manufacturing organisation, CMO) to generate formulated products that can be used in either clinical or commercial supply. The data produced is used to generate a compliant Part II/ CMC for inclusion in the submission for a marketing authorisation.

Current Model

Project management in pharmaceutical medicinal product development and registration is vital in ensuring the overall aims of the project are met. All too frequently, this responsibility resides with a single person at the innovator company who has too little time available to do it justice.

The current model for project management concerning the introduction of new pharmaceutical products to market follows the premise of a centralised project leader being the coordinator, decision-maker, planner and tracker for all aspects of the project.

A project will typically cross functions such as active pharmaceutical ingredient (API), drug product (DP) and supply chain (SC) in the development, scale-up and commercialisation phases in the life cycle.

Activity	Subject Matter Expert	Impacted Functions
Marketing need	Marketing	Project leader, R&D, regulatory consultant
API proof of concept	R&D	Project leader, Marketing
API analytical development	R&D	Project leader, Marketing
API scale-up suitability	R&D	API CMO
API CMO request for proposal	R&D, SC	API CMO
API proposal	API CMO	R&D, SC
API CMO selection	R&D, SC	API CMO
API outsourcing management	R&D, SC	API CMO
API project plan	API CMO	R&D, SC
API technology donation	R&D	API CMO
API technology receiving	API CMO	R&D
API piloting studies	API CMO	R&D
API scale-up	API CMO	R&D
API process validation	API CMO	R&D
API commercial manufacture	API CMO	SC
API continuous improvement	API CMO	SC
DP proof of concept	R&D	Project leader, Marketing
DP analytical development	R&D	Project leader, Marketing
DP scale-up suitability	R&D	DP CMO
DP CMO request for proposal	R&D, SC	DP CMO
DP proposal	DP CMO	R&D, SC
DP CMO selection	R&D, SC	DP CMO
DP outsourcing management	R&D, SC	DP CMO
DP project plan	DP CMO	R&D, SC
DP technology donation	R&D	DP CMO
DP technology receiving	DP CMO	R&D
DP piloting studies	DP CMO	R&D
DP scale-up	DP CMO	R&D
DP process validation	DP CMO	R&D
DP commercial manufacture	DP CMO	SC
DP continuous improvement	DP CMO	SC
Marketing strategy	Marketing	Regulatory consultant
Regulatory strategy	Regulatory Consultant	Marketing, regulatory authority
Data review / gap analysis	Regulatory Consultant	R&D, API CMO, DP CMO
Dossier generation	Regulatory Consultant	R&D, API CMO, DP CMO
Dossier submission	Regulatory Consultant	Regulatory authority
Response to questions	Regulatory Consultant	R&D, API CMO, DP CMO, regulatory authority
Dossier maintenance	Regulatory Consultant	Regulatory authority

Internal resource
External resource

Table 1: Project Leader Responsibility List

There is an extensive list of potential activities the project leader can be responsible for:

In pictorial terms this approach can be represented as per the diagram below.

Keeping tabs on what the marketing team need, what the development scientists are producing, and when the supplies are required in the clinic / warehouse, considering these are in-house activities, is challenge enough without having to consider what is required externally by contract development / manufacturing / regulatory support teams.

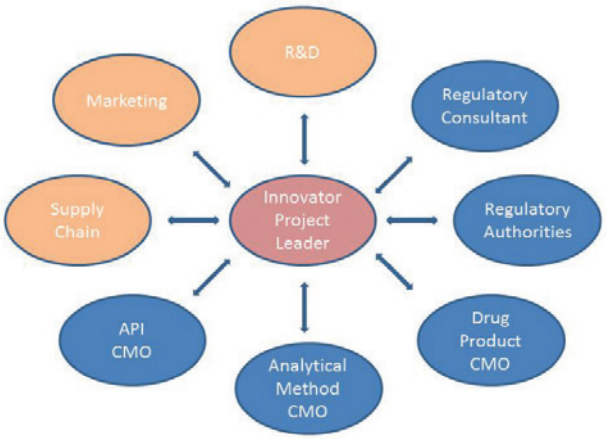

Figure 1: Current Project Support Structure

The project depicted above covers the whole range of activities, including requests for proposals; site assessments; negotiating contracts; planning activities (API and DP – probably separate organisations); regulatory standard technical packages; dossier preparation and submission to authorities.

There will also be multiple points of contact to consider as each of the key activities will have a *pseudo* project manager identified, looking after a particular area of responsibilities (e.g. at a CMO). This could be a benefit to the project leader, but frequently the CMO is more focussed on juggling the CMO resources to cover multiple projects in their facility rather than making sure any individual project runs to plan. Also, the CMO very rarely has access to the full project requirements and will therefore not be in the best position to make informed decisions.

The need for an independent project manager who has a full understanding of what is to be delivered, and is not protecting the interests of a CMO, is clear. The regulatory project manager is in an ideal role to satisfy this need, having full project oversight. The regulatory project manager would

also have the knowledge of what needs to be done during development, scale-up and manufacture to generate the quality of documents to support a regulatory dossier.

A Better Way

There is clearly a need for two very important roles within the project delivery team.

Firstly there is the project leader, who is the person with the overall responsibility for project delivery. The project leader will be an employee of the innovator who initiated the activity. The project leader will need to manage his company's needs and resources as the project unfolds.

Secondly there is the regulatory project manager, who is responsible for driving the detailed actions of the project. This role could be either internal or external to the innovator company, but in essence is responsible for ensuring good communication flow to the project leader, as well as the detailed management of the external resources required for delivery.

It is obvious that the project leader cannot satisfy both roles and needs plenty of support and assistance, and in many cases an external project manager with a focus on regulatory outcomes makes a sensible addition to the team.

The concept that a regulatory project manager is directly responsible for the external coordination of support functions and in direct communication with the project leader at all stages would address the above issue of having a single person at the hub of everything, and all decision-making going through a single person. The project leader should be responsible only for the strategic and financial decisions for the project.

Responsibilities would be broadly divided as follows:

An example of how this would look is depicted in figure 2.

Activity		Project Leader	Regulatory Project Manager
Overall project		R	I
Strategic plan linked to marketing needs and supply chain schedules		R	C
Oversight / coordination of innovator company resources		R	I
Project communication flow		R	R
API process	Proof of concept, analytical development, scale-up suitability	I	R
API CMO	Request for proposal, proposal review, selection, project plan	A	R
API technology	Document-sharing, donor and receiver management	I	R
API CMO	Ongoing management, milestone delivery, project tracking, piloting, scale-up, validation, manufacture and continuous improvement	I	R
DP process	Proof of concept, analytical development, scale-up suitability	A	R
DP CMO	Request for proposal, proposal review, selection, project plan	I	R
DP technology	Document-sharing, donor and receiver management	I	R
DP CMO	Ongoing management, milestone delivery, project tracking, piloting, scale-up, validation, manufacture and continuous improvement	I	R
Marketing strategy		R	I
Regulatory	Strategy	A	R
Regulatory	Data review, gap analysis, dossier generation, dossier submission, dossier approval and maintenance	I	R

R = Responsible, A = Approver, C = Consulted, I = Informed

Table 2: Shared Responsibility / Awareness in Improved Project Structure

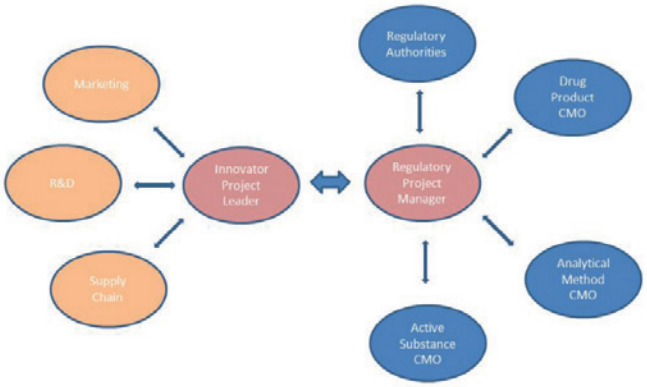

Figure 2: Improved Project Support Structure

All communications have to be two-way, accurate and timely, which is pivotal if the subject matter experts are to be kept aligned with the project goals. The key communication link is between the project leader and the regulatory project manager, and both need to be fully aligned with the project goals at all times.

The benefit of splitting the decision-making workload in this way is that the decisions are being taken not only by people who are aware of the overall aims of the project, but also aware of the specialist areas they are responsible for. This approach gives a real-time control of the compliance aspects of the projects, leading to the decisions being made with the end goal in sight and reducing the risk that a downstream regulatory gap analysis would uncover a deficiency.

An example of how this approach improves the information flow is the transfer of technology from the innovator R&D to the CMO.

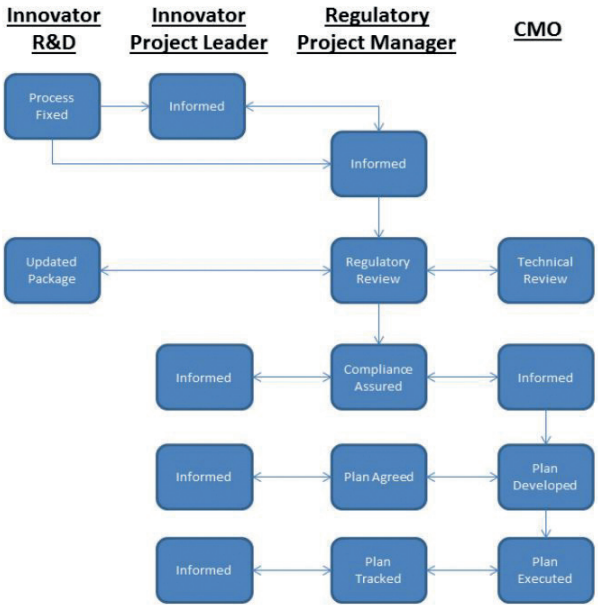

Figure 3: Example Information Flow

Instead of the information flow, as originally depicted, passing from R&D to the project leader to the CMO, the regulatory project manager will now have full visibility. This small section of a project demonstrates clearly how the load on the project leader can be reduced, but still ensures availability of full information, and the approval decisions (in this case around document transfer and delivery plan) will be the responsibility of the regulatory project manager.

Having this combined approach between the project leader and the regulatory project manager will have several benefits, such as:

- Removing the project leader as the hub of all communications
- Debottlenecking information flow
- Compliance, technical and scientific review happening in parallel
- Risks identified and mitigation strategies developed
- Compliance assured going forward
- CMO has full understanding of requirements
- Enables detailed plan to be developed and agreed
- All parties committed to plan and held to account
- Tracking to plan becomes transparent
- **Project leader kept fully informed**

A similar scenario and communication pathway could be envisaged for many other aspects of project delivery, and all would provide similar benefits to the innovator organisation. The generation of free capacity in their internal resources will mean they will be able to accommodate internal challenges / needs as required.

Selection of a Regulatory Project Manager

The key in this strategy is the selection of the regulatory project manager. The main prerequisites for being able to fulfil this role will be:

- •Regulatory experience in multiple markets (US, EU, Japan)
- CMO exposure in requests for proposals and negotiating contracts
- Hands-on experience of manufacturing at all levels (lab, pilot plant, full commercial)
- Breadth of understanding of the pharmaceutical operation (API > DP > packaged product formats)
- Scientific understanding of various disciplines (chemistry, analysis, formulations)
- Commercial acumen and understanding how to deliver marketing requests in the most cost-effective manner
- Strategic thinker
- Good communicator
- Overview of all aspects of medicinal product development in addition to Part II / CMC requirements (e.g. clinical trial management, safety and efficacy studies).

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