The role of the regulatory affairs function during mergers and acquisitions

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Abstract
Pharmaceutical companies involved in mergers and acquisitions (M&A) need to address the regulatory implications of such activity. When commercial and manufacturing aspects need to be rationalised, the regulatory affairs (RA) function must adopt a leadership role in cross-functional projects, to ensure their companies are compliant in aspects ranging from notification of site changes and product branding to the transfer of marketing authorisations and harmonisation of drug formulations. This article discusses the issues and potential pitfalls of which the RA professional should be aware, and explains the need to espouse a leadership position in such events.

Introduction
The pharmaceutical industry has undergone significant restructuring since the mid-1990s. This has been driven by major changes in the regulatory, healthcare and business environments and economic challenges surrounding the industry. Many of the major companies have struggled to increase output of their drug development programmes and have used M&A as a means of re-invigorating their product pipelines. It has also been a vehicle to increase market share, establish a presence in new and emerging markets, diversify product portfolios and reduce costs by merging commercial, manufacturing and R&D operations.

Pharmaceutical regulations dictate the need for transparency and accountability during M&A. This is usually required by declaring the legal entities and company structure responsible for the marketing, manufacturing and pharmacovigilance authorisations (among others). During M&A there is usually significant change to these legal entities requiring careful consideration of the regulatory implications and impact. Failure to consider the regulatory implications and failure to efficiently implement the necessary actions can result in serious compliance issues and threat to the continued supply of product to the market and patients.

The RA function is critical in leading and guiding the corporation through the complexities of M&A to ensure that the corporate objectives are achieved in a timely and compliant manner. The synergies derived from the M&A are publicly declared to the financial community and hence the RA function has a direct and critical role in delivering the corporate commitments.

Regulatory contribution to corporate strategy
During a classical M&A, after necessary clearance from the various governmental and regulatory authorities there is a period where implementation of the resulting corporate strategy is reviewed and agreed by senior management. The targets and objectives will be specific to each merger but a number of aspects are common to most scenarios and the consequences of such discussions can have far-reaching impact for regulatory affairs.

Typically, the following situations will have significant regulatory impact and require detailed evaluation and input from the regulatory affairs function:

Commercial rationalisation
- Immediate name change of the company being acquired (to align with the name of the acquiring company)
- Transfer of marketing authorisations (MAs) from acquired company to acquiring company
- Amalgamation of offices
- Transfer of MAs from third parties into own company commercial affiliate entities
- Change of logo and product branding
- Product rationalisation, divestment and discontinuation.

Manufacturing rationalisation
- Change in site of API manufacture
- Change in site of drug product manufacture, packaging, or release site
- Harmonisation of product presentations and pack sizes
- Harmonisation of specifications, formulations etc.

It is imperative that the RA function is actively involved and consulted during this confidential corporate strategy review. Even with minimal information, it is still possible for RA to manage high-level expectations and ensure that members of senior management are fully aware of the implications and consequences that some of their decisions will trigger.

The regulatory impact
Changes in the names and/or addresses of the companies impacted by rationalisation activities listed above will require appropriate regulatory filings in accordance with country-specific requirements. Many of the “commercial” changes are “administrative”, with no significant impact on quality, safety and efficacy. However, although the majority of global regulatory agencies treat them as such, there are still some emerging markets where a more comprehensive
regulatory submission and lengthy approval time is required (often with a dependency on approval of the changes in the "country of origin" first). Even subtle changes such as change in street address, street entrance or change in telephone numbers may need to be notified to the regulatory authorities and require pack changes, since these details are often specified in MAAs and on product packaging.

Such administrative changes may seem superficial to senior management and may cause frustration when the time taken to execute the regulatory documents and obtain necessary regulatory approvals, as well as changing the packaging, may hinder the speedy implementation of the M&A corporate objectives. It is the role of RA to carefully explain and educate senior management on the basis of the regulations and the need for compliance. It can be particularly challenging when explaining some of the long approval times in some regional markets, for relatively simple administrative changes in names/addresses and/or transfer of MA holders (MAHs).

Manufacturing rationalisation is more complex than commercial rationalisation. The former requires new quality data (often comparative batch analysis and stability data covers most markets) whereas the latter requires legal certificates and administrative applications (often based on Chamber of Commerce certificates and supporting legal letters). In both cases CPP-dependent countries (those dependent on a "certificate of pharmaceutical product") will require approval of the change in the "country of origin" first before approving the change in their own country. Consequently it is common to see a two-phase implementation plan for M&A projects. The first phase in such instances is the US, Europe and other non CPP-dependent countries, followed by the CPP-dependent countries (mainly Asia, Africa, Eastern Europe, Middle East and Latin America) in the second phase. Approvals in these CPP-dependent countries can lag behind the first phase countries by one or two years, which can cause frustration to senior management and project managers within the manufacturing and commercial functions. Once again, it is the role of the RA function to clearly explain the basis of the regulations and timescales to this audience.

Cross-functional coordination

When details of the corporate strategy emerge, it is recommended to form cross-functional project teams to ensure effective implementation of the necessary regulatory submissions and notifications in affected countries. It is absolutely critical that RA forms an effective working process and relationship within both the manufacturing function and the supply chain function. If one reviews the names and addresses of the different companies as listed on product packaging and prescribing information, one can see the correlation with the company names and addresses listed in regulatory licences and documentation. Changes to the regulatory licences consequently have to be carefully synchronised with the resulting pack changes. Every country has different timescales where packaging showing the "old" name and address must be replaced by packaging showing the "new" name and address. Efficient planning and coordination of these changes requires close collaboration between centrally-based corporate regulatory and supply chain functions and their corresponding departments in each local commercial affiliate. One single, global planning and tracking system, combining regulatory planning and the resulting pack change timetable, is crucial. Since the regulatory requirements and approval times usually dictate the timings, the RA function often takes the lead in the cross-functional project team. However, emerging requirements such as the European Variations "do and tell" procedures, switches the emphasis more on manufacturing/supply chain to plan their pack change timetable first and then ensure that RA is ready to notify the "tell" part of the "do and tell" (once manufacturing/supply chain have completed the "do" part).

Balancing the various pack changes and supply and demand switches for a large number of products across a large number of countries with such different regulatory approval times is a huge challenge. RA and the manufacturing /supply chain functions need to develop an agreed planning and tracking system database to monitor and maintain a global project plan with specified milestones. This project plan should be reviewed on a monthly basis (in conjunction with the RA, supply chain and commercial functions in the local affiliate office) to coordinate the regulatory status with the demand and supply planning process.

Since RA will see the totality of changes, they will play an important role in coordinating all changes and avoiding repeated regulatory submissions and repeated pack changes (potentially with a tremendous waste of resource and scrappage/obsolescence of packaging materials). Consider a potentially disastrous sequence of unplanned events separated in time:

- Change the company name first (regulatory and pack change 1)
- Merge office locations (regulatory and pack change 2)
- Transfer MAHs (regulatory and pack change 3)
- Change in site of manufacture (regulatory and pack change 4)
- Change in branding and logo (regulatory and pack change 5)
- ...then Commercial decides to discontinue or divest the product!

Organisation of the RA function to manage M&A projects

The RA function has a critical role, as it may be the only function that can see the totality of the changes triggered by M&A. If you consider the list of changes above, you can see that these are initiated by different areas of the business but that ultimately they will flow through RA.

RA will need to carefully consider how it organises itself to deal with the activities. Large M&As will often require separate, distinct RA groups, created specifically for the M&A. This is to ensure optimal resources and focus (with no prioritisation conflicts) are used to effect the global implementation. If a special group is created, the skills in such a group need to be considered, as the work can be a balance of labelling and CMC expertise. In such a model, the relationships and processes between the specific M&A regulatory “special projects team” and the routine RA functions within the “normal business”
need to be clearly agreed. Both functions will often be working on the same product MA, so coordination, collaboration and a prioritisation and escalation process needs to be defined.

If a “special projects” RA group is established specifically for the M&A, the future role of these individuals needs to be considered for when the M&A project is completed. It is often difficult to re-assimilate individuals back into normal line functions since the normal business and organisation may have changed significantly during the M&A years. Nonetheless, the RA individuals working on the M&A project will have acquired valuable skills and experiences and hence a transition period and re-introduction of staff into the business should be carefully planned many months prior to termination of the project.

Managing the local commercial affiliates and regulatory agencies

Affiliates: The RA function in “head office” needs to provide effective communication and forward planning for the local affiliate RA function. The local RA function has to manage the submission and review process and the interface with its regulatory agency. The regulatory agency may receive a significant increase in the volume of submissions. If both these groups are not adequately briefed they may not be able to support the overall objectives.

The importance of prompt feedback of submission and approval status of the submissions from the local RA affiliate to the central RA function and database is critical to ensure adjustments to the supply and demand scenarios and planning assumptions are visible and adjusted.

In addition to partnering with local RA colleagues for the implementation of the regulatory filings, the “head office” RA function needs to monitor compliance risks in each local affiliate office. As offices and departments are reorganised with potential job losses, the transfer of responsibilities, procedures and knowledge needs to be carefully transitioned from the old organisation to the new one. In particular, the regulatory affairs, medical and pharmacovigilance responsibilities need to be clearly defined and transferred, since failure to manage these transfers will result in serious compliance threats.

Agencies: If a significant volume of regulatory submissions is anticipated, then appropriate communications and briefings for the regulatory agencies should be considered. Resources in regulatory agencies are outside the control of the company so this potential risk area should be assessed at an early stage and considered as part of the overall project plan. Submission windows should also be considered during the planning stage, for example some agencies only accept applications one day a month; some will be closed for religious holidays; some virtually close down during the summer months. These agency-closed periods can delay implementation by months. Some agencies in “countries of origin” may be required to issue a significant number of CPP certificates to support regulatory filings in the export markets and again, the resource impact and a forward plan of CPP demand should be discussed with the relevant agencies.

The role of the RA leadership

In addition to leading, directing and organising the technical implementation of regulatory activities arising from M&A, there is also the human side. The RA leadership also needs to lead the people through times of uncertainty, change and anxiety. The perspectives can be very different if you are a leader in the acquiring company or the company being acquired. However, situations and outcomes are unpredictable during M&A and everyone should be prepared for the unexpected. The old adage, “business as usual”, is often quoted and indeed the key objective is to keep the business going while the M&A unfolds and new organisations, roles and responsibilities are established. However, it is difficult for both managers and staff to remain motivated during such a time. But this is precisely the time for leaders to step up and lead their people. They should reduce out-of-office travel and be increasingly present on the shop floor. They should encourage an open-door policy and walk the floor plate. Departmental meetings and question-and-answer sessions should be held frequently. Even when there is a lack of tangible facts and information, it is still reassuring and beneficial for staff members to have the opportunity to interact with their managers. Communication strategies and the engagement of staff are often underestimated, resulting in reduced performance, compliance issues and a loss of key talent who leave the company (often when better communication and reassurance from management may have retained them in the organisation).

The leadership also has a duty to ensure that during an organisational re-evaluation, the skills, experience and successful track record of their department is recognised and understood. Some leaders and some cultures find this easier than others. The philosophy of “Do good things and talk about them” does not come easily to some leaders and cultures who are focusing solely on delivering the results – but then their achievements and track record may not be visible to new management. Although sometimes unpalatable, it is the role of the leadership to focus on such aspects which may require development of slide decks, brochures, posters, annual reports, etc. This is usually accompanied by a period of departmental “housekeeping” in readiness for an audit or evaluation by the acquiring company or third party consultants.

Conclusion

The RA function has a critical role during M&A. Significant corporate objectives requiring commercial and manufacturing rationalisation will trigger global regulatory implications. The RA function needs to establish a leadership position in such cross-functional activities and projects, since the regulatory timelines and the successful achievement of regulatory approvals will dictate the timing and achievement of the corporate objectives.

In addition to leading the necessary regulatory activities, the RA leadership has a critical role in leading and guiding its staff through the inevitable changes arising from M&A situations. This period can often be the most demanding and important time of a leader’s career, as wholesale organisational changes can often have significant impact (both positive and negative) on careers and individuals.

RA leaders who can successfully negotiate both the technical and human aspects of M&A situations are invaluable to any organisation.