BY ROBIN ROBINSON

REGISTRATION AND LAUNCH: The Next Steps of a Long Journey

The expanding global market is creating hurdles within the registration process, requiring long-term views and solutions to bring a product successfully to launch.

NANCY SMERKANICH ■ *Octagon Research Solutions*

Technology is assisting in the review of submission documentation at the FDA, as well as the review of supporting submission data."

ED DAMP ■ *BioPath Consulting*

One of the best practices to prepare the market for launch is to make physicians aware of the gaps in the current treatment of the disease."

FAST FACT

TOTAL TIME FROM PROTOCOL DESIGN READINESS TO DATA LOCK ROSE 70%, FROM 460 TO 780 DAYS, BETWEEN THE EARLY AND MID-2000S.

Source: Tufts CSDD

The registration and launch phase is evolving like the rest of drug development, and the industry must evolve its practices along with it. One big aha moment for the industry is to understand that data, study reports, and other regulatory documents are not the end, but rather integral parts of the journey. New regulations, new electronic submission requirements, and the increasing need for global submissions are keeping industry stakeholders on their toes.

Registration: Challenges

As of June 2009, FDA regulations require the electronic submission of drug registrations, listings, annual renewals, and updates of OTC drugs, active pharmaceutical ingredients, prescription drugs, homeopathic drugs, and animal drug products.

As the transition from paper to eCTD (electronic common technical document) continues, drugmakers face a medley of requirements depending on the level of drug development. Combine those requirements with diverse regional and national data requirements, and the registration environment becomes highly complex. While technology is becoming an integral part of the registration stage and is the key for ensuring timely review of NDA/BLA submissions, adoption is not without its challenges.

In addition to the technology required to build submissions on the side of the sponsor, the ability to validate and view the submission on the FDA's side is key, says Nancy Smerkanich, executive VP, global regulatory affairs, at Octagon Research Solutions.

"Technology is assisting in the review of submission documentation at the FDA, as well as the review of supporting submission data," Ms. Smerkanich says. "Through the employment of data standards, such as the CDISC's SDTM, the FDA has been able to use e-review tools, such as a patient profile viewer and WebSDM, to facilitate electronic review tasks."

According to Anne Tomalin, president of i3 CanReg, there are a number of technology solutions that can be used to compile and submit these applications so that they comply with regulatory specifications.

"Similarly, the ability to provide labeling in a structured product labeling (SPL) format in the United States and its counterpart in Europe is essential," she says. "Using technology that allows safety data to be compiled and searched in an appropriate manner to answer questions from regulatory agencies will help speed the registration process. Likewise, the use of MedDRA dictionaries to code safety information ensures that similar ADRs across languages are appropriately filed."

Submissions can also be made more efficient by using electronic software and eCTD lifecycle management tools, Ms. Tomalin says.

"These tools not only help keep data in order, but allow for better searching of data to address questions that may arise," she says.

Other best practices include working with regulatory bodies on developing strategies for preclinical/clinical data, because agencies involved in strategy development are more likely to accept the data that are generated.

"Global regulatory teams that can help address the needs of local markets and take the decided strategies forward for discussion can help guide submission development," Ms. Tomalin adds. "Clear guidelines developed through ICH or joint regulatory agencies help define the path and lead to less duplication because of local differences."

Another way to improve the efficiency of submissions is to conduct more content planning, says Loni Jakub, manager, ViewPoint Implementation Services, Octagon Research.

"Many product development teams don't appreciate the importance of content planning

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DONNA MICHALIZYSEN ■ *Precept Medical Communications*

Moving forward, we must transform our dialogue with KOLs from single interactions to developing an ongoing relationship."

for a submission until they experience the chaos of tracking and managing hundreds of documents in various stages of completion, coming from multiple sources around the globe, inundating the submission team," she says. "The team that takes a hard line on content planning will be much better positioned to produce the submission in an efficient and timely manner."

But no matter how much planning is done, there are bound to be unforeseeable activities that stall even the best submission plans. When reactive changes and decisions are made under less-than-optimal circumstances, they are often communicated by e-mail or phone and not properly documented.

"This only adds time and contributes to team frustration when attempting to respond to agency queries post-submission," Ms. Jakub says. "By taking the time to implement a standard process and technology mechanism to capture planned content decisions and processes as well as unplanned issues with appropriate resolutions, the project team can continue to operate like a well-oiled machine throughout the peaks and valleys of submission assembly and move in a positive direction for continuous process improvements for future submissions."

By coupling eCTD regulatory standards with a sponsor's guidance interpretation, technology can be leveraged to fill in the missing gaps in content authoring and varying regulatory guidelines. This further exploration of technology can help identify content sections that

can be reused and help sponsors acknowledge assembled components that can be included in several health authority deliverables.

Registration: Global Submissions

Global registrations present another list of challenges. The tasks of interpreting, managing, and communicating varying regional and local requirements continue to challenge sponsor organizations as they pursue global registrations, Ms. Jakub says.

New markets such as India and China are becoming important for global registration, and companies need to learn how best to approach these regulatory agencies.

"The industry is definitely evolving its practices regarding registration and launch," Ms. Jakub says. "Organizations are starting to understand that data, study reports, and other regulatory documents are not final products, and that ultimately these items will be included as components for multiple regulatory submissions around the globe. Submissions need to help tell a story for each health authority, and they need to be consistent and compliant with data and submission standards, as well as provide an opportunity for reuse."

Ms. Jakub explains that as the industry continues to move toward global simultaneous submissions — a phase that has yet to be fully realized for the majority of sponsors — consistent processes, streamlined technologies, or single authoritative sources can be leveraged to enhance an organization's capacity to reuse submission content for a given drug product for inclusion in multiple submissions.

"eCTD provides a standardized format and regulatory guidelines to move a step closer to near simultaneous submissions, but these requirements still vary among health authorities and require a reimagining of content sections from the sponsor," Ms. Jakub adds.

Most global companies experience a disconnect between headquarters and affiliates in terms of information flow about regional regulatory requirements, what was actually submitted, and what next steps should be for a specific regulatory filing, she says.

"This information divide is often exacerbated by disjointed systems and processes that leak remnants of information but don't tell the whole story about a product's regulatory life cycle," Ms. Jakub says. "It's not enough to manage just the metadata, such as date submitted, main points of contacts, and approval dates; one has to know where to find the data within the submission. Most often, the answers exist within sections of submitted documents, and pulling out this information is like a treasure hunt. As a result, a sponsor organization can spend significant time and energy locating the information and connecting the dots rather than communicating the solution."

According to Ms. Tomalin, as agencies around the world begin to communicate with each other and new communication links are used to share thoughts regarding data review, a more integrated approach to global registration will emerge.

ANNE TOMALIN ■ *i3 CanReg*

Using technology that allows safety data to be compiled and searched in an appropriate manner to answer questions from regulatory agencies will help speed the registration process."

TRANSATLANTIC REGULATORY INTEGRATION

According to a recent Frost & Sullivan report, regulatory processes differ across continents, posing challenges to drug launches. There is a pressing need to integrate the regulatory environments of the European Union (EU) and the United States. Diverse regulations impact drug launches as less price-controlled markets witness quicker launches, while it takes longer in regulated markets. The pharmaceutical industry, along with regulatory agencies, has been working closely with the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) to develop a standard set of regulatory processes for Europe, the United States, and Japan.

Pan-European integration and transatlantic coordination on the regulatory front is high on the agenda for Europe, Middle East, and Africa (EMEA), and the FDA.

Source: Frost & Sullivan. For more information, visit frost.com.

Launch: Prepping the Market

One best practice to prepare the market for launch is to make physicians aware of the gaps

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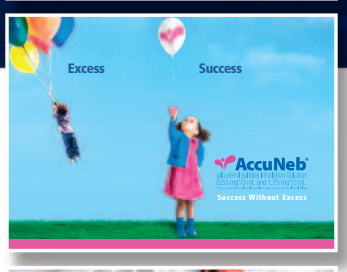

in the current treatment of the disease, says Ed Damp, chief operating officer of BioPath Consulting.

"Multiple channels can be used to close this gap; one of the most effective is the salesforce," Mr. Damp says.

For this, sales reps need to be able to communicate with physicians on a peer-to-peer level and consult with physicians regarding what gaps in treatment are present and how those gaps need be filled.

"Since sales reps are not allowed to discuss nonmarketed products with healthcare professionals, companies need to provide training and education on how to talk about the gaps," Mr. Damp suggests. "This will lay a strong foundation for the drug when it is launched and becomes marketed. The ability for the sales reps to be able to consult physicians during this period is crucial to developing a working relationship that will grow stronger leading up to the product launch."

Preparing the salesforce for launch will require more in-depth education in terms of scientific and clinical training.

"Field forces can no longer memorize a marketing message; reps will need to become experts in their disease and therapeutic area, and be able to discuss these topics with physicians from a consultative perspective, rather than a sales one," Mr. Damp says. "They need to demonstrate that they can be consultative and work with physicians to determine the best treatment options for patients to provide the best outcomes. Unfortunately, these options will sometimes be competitor products, but at least the field force will prove to physicians that they are valuable assets who can be trusted and relied on."

"In current organizational thinking, one of the changes that must occur is the recognition that relationships matter," says Donna Michalizysen, managing partner, Precept Medical Communications. "Moving forward, we must transform our dialogue with KOLs from single interactions to developing an ongoing relationship. Actively and continuously engaging an expert throughout the prelaunch stage, for example, can provide opportunities to uncover unique observations that may help to identify new data, novel analytical methods, and potentially identify unique outcome measures or additional endpoints to include in ongoing trials. These actions will help define new ways therapies can be used to improve healthcare and, ultimately, strategically differentiate the products. Often these perspectives are left undiscovered because the two-way communication channels are not formalized and information we share with KOLs is incomplete at best."

To improve the ability to uncover key insights and act on them, a process to collect and share collective insights must be created.

"Optimizing the collective insights gathered from KOLs requires drawing important inferences from discussions that are fragmented because they occur over the course of years and/or are driven by different functional groups — clinical, medical, marketing — within an organization," Ms. Michalizysen says. "Many times, the insights necessary to strategically differentiate products and fully optimize their strengths are within reach but remain hidden due to this fragmented approach."

LONI JAKUB ■ *Octagon Research Solutions*

Many product development teams don't appreciate the importance of content planning for a submission until they experience the chaos of tracking and managing hundreds of documents in various stages of completion, coming from multiple sources around the globe."

Fewer drug approvals and increasing regulatory demands have companies turning their attention to building productive relationships with KOLs and supporting company objectives through medical education. MSL staffing is critical right before and after a drug's launch. New drugs could mean new research opportunities, and MSLs are the most likely initial resource for introducing a new drug and its safety and efficacy information. It is important, our experts say, to not overlook the value of the MSL role in this phase.

"To improve communications between MSLs and physicians during registration, MSLs, medical affairs, and medical information services should build a library of information and resources," says Robin Winter-Sperry, M.D., president and CEO, Scientific Advantage and Science Oriented Solutions (SOS). "The company's medical experts should have an intimate understanding of data, be in sync with key cross-functional areas internally from a strategic standpoint, and actively educate thought leaders in the medical community to lay the foreground for the agent's introduction.

"An important part of launch readiness should be an educated audience that is aware of the agent in development and anticipates it," she adds. "The medical community should also be educated about the disease state and clinical data — with no claims about safety and efficacy prior to regulatory acceptance — in anticipation of launch."

As products move closer to launch, each marketing channel needs to be optimized to create the greatest impact on new patients. Allocating the spend or focus among the many launch activities — speaker training programs, CME, thought leader development, direct-to-consumer, direct-to-physician, marketing salesforce communications — can be a difficult task when preparing for a launch.

According to Dr. Winter-Sperry, companies should look at the target audience, anticipate educational opportunities, identify areas of greatest need, and review the impact potential of what they discover to align the resources and prioritize accordingly.

Thought leader development and medical education are always essential, she says; however, the uniqueness of the product, the medical urgency associated with it, corporate portfolio, and depth of company resources will also have a major impact on the company's ability to create a launch-ready environment and implementation strategy. She says companies can develop medical education through non-CME programs that are directly supportive of their new agent and disease state.

Trevor Fitzpatrick, VP and general manager, medical communications services, at Parexel International, offers up some "next practices" that should be considered for more successful product commercialization.

First, Mr. Fitzpatrick suggests fostering improved integration between R&D, medical, marketing, and training functions to catalyze evidence-based communications of greater educational value. Second, he advises that the industry align its strategies with healthcare professionals' own priorities for data, tools, and access to knowledge. Third, gold standard medical communications should incorporate faster reaction times to a rapidly changing environment, especially with regard to compliance guidelines, the potential of social media, and the needs of payers and regulators. Finally, medical communications are especially important against the backdrop of an increased demand for health outcomes evidence and a greater focus on CER, REMS, and personalized medicine.

"Overall, medical communications must increasingly deliver customizable, on-demand education tailored to the needs of each audience," Mr. Fitzpatrick says. ✦

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SPEAKERS

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