Tackling Pharmaceutical Industry’s Regulatory Affairs Challenges with Technology
Introduction
The success of a pharmaceutical manufacturer depends upon the effectiveness of its Regulatory Affairs (RA) department. RA professionals in the pharmaceutical industry play the critical role of ensuring that a manufacturer is in compliance with regulatory bodies from pre-launch through the entire product life cycle.

This is no easy task. During the product development phase, RA professionals must ensure that procedures are aligned with current country-specific regulatory requirements, facilitate internal and external audits to uphold the quality and integrity of trial data and processes, and maintain appropriate documentation in order to demonstrate the standardization and harmonization of regulatory processes to the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA) and other regulators.

Post-approval, pharmaceutical RA professionals must continue to interact with local authorities and maintain documented, up-to-date regulatory procedures so that manufacturers can market and sell products in compliance with governing bodies. A critical component of this work is ensuring that products are properly registered in the markets in which the manufacturer is selling them. This involves not only securing initial product registrations but also keeping them up to date and submitting changes to registrations when deemed necessary by the regulators, all of which have individual rules, requirements and timelines.

The product registration process must be closely aligned with the change control process so that RA professionals can analyze and measure the impact of product changes to determine when they must secure new product registrations or updates. Throughout the process, RA professionals must also manage and track correspondence and commitments with regulatory bodies to ensure required actions are logged, assigned and completed in compliance with specified guidelines and deadlines.

This paper examines the demands of product registration in the global pharmaceutical marketplace, the challenges RA professionals face when attempting to comply with the guidance and rules of various regulators and technology solutions that are available to reduce the costs and risks, while increasing the efficiency and accuracy of product registration tracking (PRT) and related processes.

Product Registration: A Matter of Process
While on the surface the act of registering a drug with a regulatory authority appears to be a straightforward, stand-alone, document-centric task. A closer look reveals a complex process contingent upon a broad range of activities, both inside and outside of the RA department.

Vast amounts of information in different locations
A single product registration in a single market requires a manufacturer to provide varied and detailed information on the drug intended to be sold, such as clinical trial data, specifics on the formulations, modes of delivery and dosages, indications, manufacturing details (who manufactures the ingredients and where), quality control specifications, as well as packaging and labeling materials. Typically, this information is not housed in a standardized format in a single repository. It is owned and managed by different departments with the organization (RA, quality, manufacturing, etc.). When one considers that most pharmaceutical manufacturers sell not just one product to one market but multiple versions of multiple drugs across a broad range of markets, the complexity of data collection, reconciliation and submission process becomes clear.

An active process
Product registration is not a one-time event. Most health authorities require manufacturers to update product registrations on a regular basis (e.g., bi-annually, semi-annually, or annually). Furthermore, regulators typically require a manufacturer to re-register a product when changes such as a revision to the formulation, indication, administration route, packaging or labeling are introduced.

Product registration in the pharmaceutical industry is a complex process that must be actively managed by regulatory affairs. A critical component of this is change control. To ensure that the safety, quality, purity and potency of drug products are not compromised by production and process changes, a manufacturer must place organizational systems that evaluate changes, track them and communicate them to those who are affected by that change. This includes RA professionals who must be alerted to changes in product specifications, production processes and associated documentation so that they can determine if these changes necessitate new product registrations or updates.
Different markets, different requirements
Adding to the complexity of the product registration process are the considerable variations in guidelines, regulations, timelines and deadlines set forth by regulators across the globe. In a recent study of registration procedures across 12 countries, researchers found that while many of the application requirements were similar, the differences in the requirements for product registration, the initial evaluation and renewal processes varied—including costs of registration, quality analysis requirements, the length of evaluation processes, the duration of registration certificates, renewal policies and GMP compliance. While the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) offers pharmaceutical manufacturers standard guidelines for submitting product registrations in Europe, Japan and the U.S., the procedures around registrations in these markets can vary widely.

For example, there are four different ways a manufacturer can secure market authorization in an EU Member State with state-specific requirements:

- **National Procedure (NP)**
  Used when a standard application is made for the first time in a single member state (EU)

- **Mutual Recognition Procedure (MRP)**
  Means that EU countries may approve the decision made about a product by another EU country

- **Decentralized Procedure (DCP)**
  For products that have not yet received authorization in any EU country, and would like a mutual recognition

- **Centralized Procedure (CP)**
  Used for product authorization in all EU countries through the EMA

When one considers these and other differences in product registration regulations, it is evident that RA professionals face significant challenges in meeting country specific requirements and tracking multiple submissions through multiple countries when launching new products or entering new markets.

Managing correspondences and commitments
Not only must RA professionals manage the product registrations themselves, they must also track all correspondence, responses, resulting commitments and any action items required to ensure proper closure of outstanding registration issues with regulatory authorities. With regulatory authorities imposing diverse timelines and deadlines for various actions and approvals, a standardized, centralized management system is critical.

The role of regulatory affiliates
To manage the PRT process in each country and region in which products are sold or distributed products, global pharmaceutical manufacturers typically rely on regulatory affiliates that understand the nuances of the local submission process, requirements and timelines.

When a manufacturer prepares to market a new, updated or revised product, it notifies the regulatory affiliates in which the product will be sold or distributed so that each affiliate can properly register the product with local regulatory bodies. Following the initial registrations, the affiliates, under the authority of the manufacturer, are responsible for managing all activity related to the manufacturers’ product registrations within their market, including the filing of regular registrations (e.g., bi-annually, semi-annually, annually), updating current registrations to meet the changing regulatory requirements and submitting new or re-registrations following a product change.

Because these affiliates are third parties operating remotely and not employees of the pharmaceutical manufacturer, RA professionals frequently experience challenges in timely and accurate tracking of their activities.

Product Registration Tracking Today: Manual, Disjointed and Prone to Errors
While PRT is vital to a pharmaceutical manufacturer’s operations, ensuring that a company can legally sell products within specific markets, most RA professionals today manage the requirements, information, deadlines, correspondences and commitments using manual, disjointed processes that are inefficient and prone to errors.

The conventional approach is to use what is commonly referred to in the pharmaceutical industry as “trackers,” which are Excel spreadsheets into which RA professionals manually record where company products are registered in the world, the activity of regulatory affiliates, critical timelines and deadlines for re-registrations and updates, communications with regulatory bodies and agreed upon commitments for compliance. In the case of one global pharmaceutical manufacturer, its RA department had over 200 trackers managing the registration of drugs throughout the world.

The manual process extends into communication with local affiliates as well, with RA professionals emailing or calling affiliates
to relay product changes and obtain updates on registrations. This can require full-time resources to manage the administrative process. Without an electronic solution in place, RA professionals must rely on contracts with the affiliates to ensure that products are properly registered for sale/distribution in various markets across the world.

The drawbacks of this approach
Envision a global pharmaceutical manufacturer that is changing the supplier of one inactive ingredient in a drug product that is marketed in 15 different dosages in 88 locations across the world. In order to implement the change, the RA professional is responsible for updating 1,320 product registrations globally for a single product change. An RA professional employed by a manufacturer with multiple divisions, hundreds of product lines and thousands of products could potentially face tens of thousands of product registration changes in the course of a year (see Chart 1).

Case in Point: A Representative Global Pharmaceutical Manufacturer
- 8 Product Lines
- 13 Products
- 88 Global Regulatory Affiliates
- 9152 Product Registrations to Manage Across the World

Managing data and processes manually presents a number of significant problems from sheer inefficiency and the cost of labor required for manual data entry to the risk for errors and the liability that a manufacturer faces when a drug product is not properly registered for sale/distribution with a local regulatory body.

Inefficient processes
The process of identifying, collecting and normalizing the product information required for registration, renewal or re-registration presents a significant burden when performed in a manual way. Because the required information is owned and managed by different parts of an organization, and not just regulatory affairs, RA professionals spend a great deal of time and effort chasing down data needed to perform the task.

An equal or even greater burden is manually tracking the status of a manufacturer’s product registrations across the globe and the activities required to be in compliance in each market. Today, RA professionals are typing information into columns and rows of spreadsheets in an effort to keep on top of where products are registered, what correspondence has taken place with local regulators, what commitments have been made, what must be done and when to keep in compliance, who is responsible for specific tasks, and whether specific tasks have been completed. Because there are typically multiple versions of these trackers floating around a company, with internal staff swapping files with each other and with local affiliates, RA professionals spend countless hours reconciling the various versions in an effort to manage the data stream.

Consider the RA professional referenced earlier who is faced with updating 1,320 product registrations for a single product and it is clear that the complexity and inefficiencies of the product registration process in a manual environment are enormous.

Lack of data integrity
Without a single source of truth for product registration status, RA professionals run the risk that they are making decisions based on erroneous and/or outdated information. Furthermore, with multiple parties, both internal and external, accessing and changing the data within the same spreadsheets, the risk of noncompliance rises with health authority regulations because of the inability to provide an audit trail. Regulators are likely to question the validity of a manufacturer’s product registrations when uncontrolled access to the spreadsheets is given and a history of changes to the data cannot be established.

Lack of visibility and control
In a manual environment of spreadsheets, with no single source of truth and questionable data integrity, RA professionals do not have real-time visibility into product registration status. For example, a manufacturer with 200 trackers leaves the RA professional with the task of reconciling the data contained within those multiple trackers. By the time he/she completes this process, information is already outdated because product registration status shifts from day to day as registrations expire, requirements evolve and local regulators request additional information.

Another challenge to managing PRT manually is the inability to integrate with the manufacturer’s change control process. Without a way to be proactively alerted to product changes that affect registrations, RA professionals must constantly investigate changes that have taken place and whether new registration or revision is warranted.
This lack of visibility also extends to a manufacturer’s interactions with local affiliates. In a manual environment of spreadsheets, an RA professional has little visibility into the activity of local affiliates beyond what the affiliates are communicating to him/her. An affiliate might report that it submitted additional information to a local regulatory body, but the RA professional using manual processes has no efficient way to confirm this activity. He/she also has no effective way to evaluate the performance of each of its company’s affiliates and perform a comparison to determine which affiliates are performing adequately and which are underperforming. In a manual environment, RA professionals lack control over key regulatory activities that are the lifeblood of the company’s operations.

Risks and Costs

It is an understatement to say that manual, disjointed and error prone processes are inadequate for managing this critical component of an RA professional’s responsibilities. A manufacturer cannot sell a product within a market unless it is properly registered with the local regulatory authority. Failures in PRT pose considerable risks and can lead to significant costs.

For instance, if an RA professional has determined that one of his/her company’s products is being sold in a major market unregistered because his/her team failed to properly register it or failed to complete a renewal, the manufacturer would likely have to recall the product until the registration issue was resolved. This situation can quickly lead to considerable financial losses from the cost to store product until it can safely be distributed back out into the marketplace to the loss of market share that occurs when customers turn to competitor products—with some likely to make a permanent switch.

A potentially greater challenge is presented when a manufacturer is confronted with a situation where the control of the product shifts, such as when the manufacturer ships drugs to a market only to be notified by the regulatory authorities that products have not been properly registered. Cases exist where authorities have quarantined temperature-sensitive drug products in warehouses with no temperature controls as the manufacturer works to secure the proper registration. The manufacturer must then decide whether products can be sold or must be discarded—and how to absorb the loss.

An Enterprise-Wide Approach to Product Registration Tracking

The product registration process in the pharmaceutical industry is both global and local. RA professionals must ensure compliance with local regulations and maintain global visibility and control over product registrations throughout the world. This can be facilitated through an enterprise-wide approach to PRT and related processes that leverage automation and integration.

Below are the key features/capabilities required of such a system to overcome the challenges faced by RA professionals today. In today’s competitive environment, RA professionals must be able to quickly answer three critical questions:

- What can we sell where?
- When can we sell it there?
- Do we owe the regulators anything?

Global visibility and control with local, customizable access

With multiple parties in various locations across the globe managing the product registration process for a single pharmaceutical manufacturer, it is critical that RA professionals implement a central solution that all users can access. Company employees and third party affiliates must be able to share information and work collaboratively together in a real-time manner. Furthermore, a common, collaborative platform offers RA professionals a global view of all product registration activities across the manufacturer’s product portfolio and markets, creating a channel to proactively identify and address potential concerns (e.g., expiring registrations, pending commitments) before they become major issues.

Rather than forcing users to adapt activities to conform to system requirements, a PRT solution should be configurable and flexible to meet local needs but still feature global views and reporting. This allows for RA professionals to ensure that all parties are meeting the necessary requirements and deadlines to maintain compliance and minimize organizational risk. For example, the solution should provide local users with customizable templates for correspondence with local regulators with support for different languages. Standardized documents and workflows that can be adapted to meet local needs enable RA professionals to drive greater efficiency and accuracy throughout the PRT process.

Because regulatory requirements are constantly changing, the solution should be easily updateable so that RA professionals can keep pace with the change. For example, when there are changes to a regulator’s e-reporting standards, the solution vendor should provide timely updates to ensure users are generating reports in the correct formats.
System and data integration
An ideal solution for PRT should integrate with a manufacturer’s core business systems (e.g., ERP) and automatically draw the required data for product registrations so that RA professionals and local affiliates can quickly and accurately fulfill regulatory requirements. This not only eliminates the need for manual data entry but also ensures that regulatory affiliates are using accurate, consistent and up-to-date information when registering or re-registering products or making changes to existing product registrations.

A PRT solution should also directly integrate with the manufacturer’s global change control process so that it can alert users to product changes that may affect registration and correspondence activities. Ideally the solution should also automatically generate registration/correspondence records required to update registrations in those markets impacted by the change.

In addition, the solution should integrate with the manufacturer’s document management system, publishing and submission software, and safety reporting system, as well as provide users with electronic access to original documents so that correspondence with regulatory authorities, resulting commitments and product safety update reports (PSURs) can be managed and tracked.

Process automation
One of the greatest challenges for RA professionals managing product registrations in a manual environment is keeping track of all of the processes and information around the actual submissions—the regulatory deadlines, tasks to be executed, commitments made to health authorities, each agency’s rules, requirements and timelines, and submission procedures. This can be solved through automation.

A PRT solution should incorporate business rules and knowledge to alert users to deadlines in advance of 30, 60, 90, or 120 days, enabling them to proactively assemble the necessary information and avoid last minute scrambles and delays. This should include the ability to configure the system so that it walks users through the necessary steps to satisfy a regulatory requirement. For example, when a user is required to submit a product registration to a particular regulatory agency, the system should generate a set of tasks that must be completed along with the corresponding deadlines, so the responsible individual understands exactly what must be executed and in what order.

An intuitive interface and configurable reporting
Because effective product registration management is critical to a pharmaceutical manufacturer’s operations, with sales hinging on the successful execution of registration processes, RA professionals must be able to leverage PRT solutions to gain accurate and timely insights into activities across all markets in which products are sold.

The solution should feature an intuitive, user-friendly interface, and search and report tools that enable RA professionals to easily identify:

- All product registrations by country
- Current product registration status
- Product registration due in 30/60/90/120 days
- Expired product registrations
- Pending regulatory authority activity
- Whether all products are properly registered and authorized for sale

RA professionals should also be able to leverage the system to quickly and easily generate reports to evaluate the effectiveness of their product registration activities. The solution’s reporting tool should enable full customization so that users can generate reports to meet the needs and preferences of various audiences, from management to power users.

Increase Visibility and Take Control
With a single, automated, electronic PRT process, RA professionals can take control of product registrations across the globe and know in real-time which products are registered for sale/distribution in specific markets at any given time.

With the ability to see exactly where their products are currently marketed and distributed, RA professionals can strategically drive competitive product portfolios based on where there are the greatest profit margins and on successful product types and corresponding markets.

RA professionals can also prioritize workloads by viewing only the countries, regions and products pertinent to particular tasks. With visibility into the activities of local regulatory affiliates, RA professionals can understand the competence and effectiveness of each affiliate, compare performance and make educated
Sparta Systems, an industry pioneer and leading provider of enterprise quality management software (EQMS) solutions, enables businesses to safely and efficiently deliver their products to market. Its TrackWise® EQMS, a trusted standard among highly regulated industries, is used by quality, manufacturing and regulatory affairs professionals to manage compliance, reduce risk and improve safety across the global enterprise. Headquartered in New Jersey and with locations across Europe and Asia, Sparta Systems maintains an extensive install base in the pharmaceutical and biotechnology, medical device, electronics manufacturing and consumer products markets.

To learn more about this topic and how Sparta Systems can help, visit www.spartasystems.com

Global Headquarters
200 Waterview Drive
Hamilton, NJ 08691
(609) 807-5100
(888) 261-5948
info@spartasystems.com

European Offices
Berlin | London
europe-info@spartasystems.com

Asia Pacific Offices
Singapore
apac-info@spartasystems.com