COMPLIANCE – THE COMPETITIVE DIFFERENTIATOR TO COMMERCIALIZATION:

An Integrated Model Setting the New Global Standard

Vikram Anand, PMI, MBA,
Executive Vice President, Life Sciences Compliance

Thomas Barton, *Associate Vice President, Business Transformation*
Larry J. Davis, ***PharmD,*** *Vice President, Medical and Clinical Affairs*
Nina Lahanis, *Associate Vice President, Pharmacovigilance*
Carolyn Quon, PharmD, *Vice President, Medical Communications*
Lisa Rinker, *Senior Director, Pharmacovigilance*

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This white paper demonstrates how integrated life sciences compliance has earned its seat at the table by demonstrating the value of increasing data-driven and technology-infused competitiveness in the successful commercialization of a new-age biopharma product. Through the lens of an integrated pharmacovigilance, medical affairs, regulatory and quality team, we'll outline the challenges manufacturers face in bringing a brand to market; detail how the integration of services, process and technology leads to increases in safety and efficiencies; and stress the importance of moving compliance from a cost center to one of value and insight. As part of a larger commercial platform, we will define how this holistic approach is fast becoming the new global standard of compliance that proves to be the competitive differentiator to commercialization.

Global Market Dynamics Create a Need for a New Compliance Model

Compliance is an integral part of the entire biopharma, medical device and SaMD (Software as a Medical Device) product lifecycle, yet it poses one of the biggest challenges for our customers: They want to focus on driving value, innovation and patient centricity but find that much of their efforts and finances are still being invested in managing regulatory obligations.

Challenges are spread across internal factors, such as obsolete and disconnected platforms, multiple silos and manual processes, to external factors like the changing regulatory landscape and increased scrutiny of regulators. Competitive forces leading to innovatively deploy the latest R&D technology to better understand and influence patient behavior throughout the patient journey add further complexities to managing end-to-end compliance.

These challenges prevent our customers from moving the needle of compliance from cost to value. **FIGURE 1** shows how we've condensed these market dynamics into the four categories – identifying the biggest challenge for customers as siloed vendors, which leads to inefficiency across operations and technology, and the inability to drive true value from data and taking end-to-end accountability for real impact on better drugs and patient centricity.

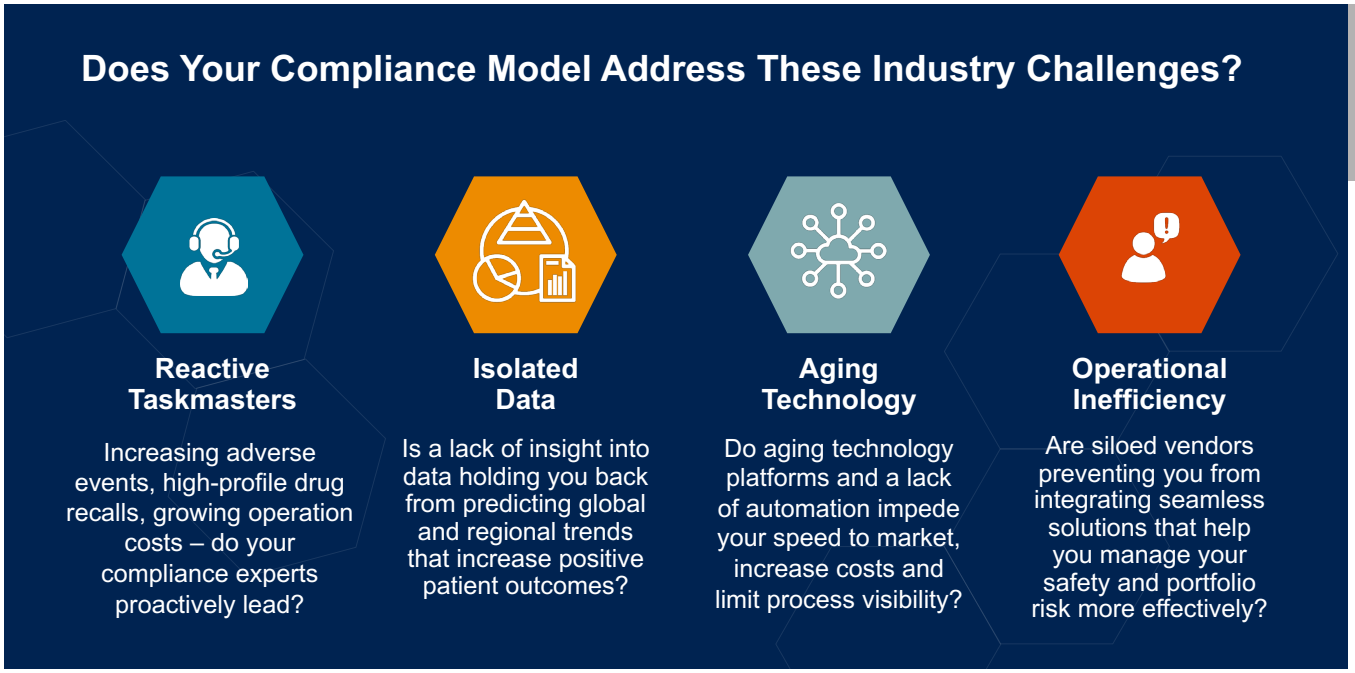


FIGURE 1

Owning and driving solutions from strategy to execution to the impact in value creation via end-to-end compliance is the differentiating path forward and one that ensures that companies are regulatory inspection-ready 365 days of the year with no surprises and dead investments into regulatory gaps or handling other similar challenges in a reactive manner. Embedding the entire compliance framework into the culture of the organization and contributing as one of the leading forces for innovating and bringing better drugs for the patients is key for commercial success.

FIGURE 2 identifies the five value creation areas we've implemented throughout the compliance paradigm to drive this holistic approach:

1. Integrating technology and automation
2. Driving value out of the data through proactive analytics
3. Streamlining and integrating processes for efficiency and better productivity
4. Ensuring regulatory inspection readiness 365 days a year
5. Evaluating enterprise risk/benefit associated with a product or a portfolio in real time

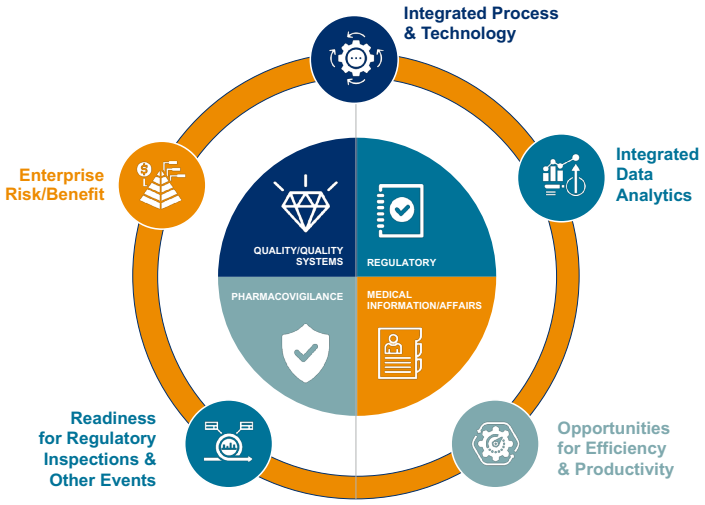


FIGURE 2

From a compliance perspective, this model comprises the four integrated services in **FIGURE 2**: Pharmacovigilance, Medical Information/Affairs, Regulatory, and Quality Assurance and Quality Systems. Within a larger commercial platform, such as that offered by EVERSANA, Compliance is integrated within Patient Services, Channel Management, Data and Analytics, Digital Medicine and Field Solution services. This new global approach as a single partner brings the best solutions across business processes, technology and people into one integrated solution that is flexible and can be right-sized for different sizes and types of organizations.

On the next page, **FIGURE 3** highlights how this model can be scoped from setting up an integrated/centralized compliance monitoring center across the four service lines or supporting customers in one of the process areas. In terms of value creation, this model supports companies at the operational level, ensuring ongoing regulatory compliance – helping to create true value through proactive and predictive data analytics and delivering on all five value creation areas indicated in **FIGURE 2**. Who would you prefer to work with: an outsourced vendor or a true partner delivering a value-based, integrated model across Quality, Regulatory, Pharmacovigilance and Medical Affairs?

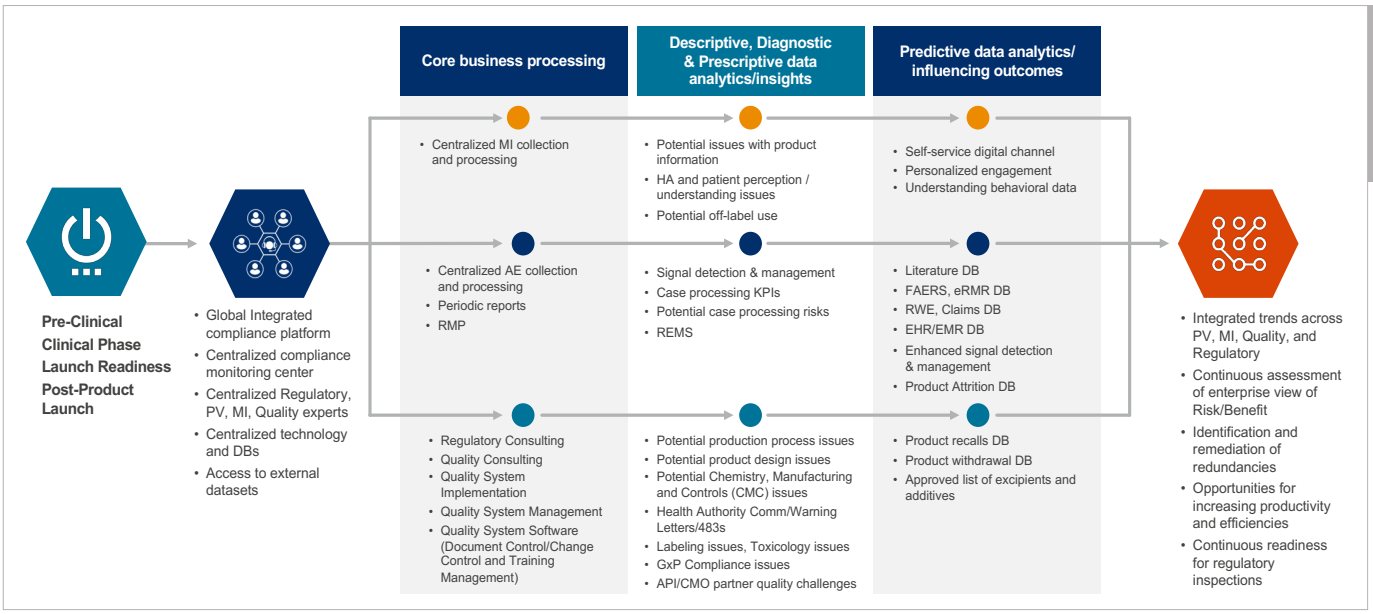


FIGURE 3

This launch model also incorporates the importance of leveraging technology that can vastly improve both efficiency and quality – namely, technology solutions in the broad categories of integration and automation. This technology can be implemented synergistically to remove most manual tasks throughout the compliance workflow to dramatically reduce overhead costs and eliminate the types of processing errors that only occur with manual processing methods and lack of system integrations.

The key outcome of any automated solution should be maximized efficiencies and cost reduction with a corresponding increase in quality and data integrity achieved through the reduction of manual tasks. With the right goals in mind, finding the "best fit" automation and integration solutions for your organization should not be difficult to achieve. A knowledge of the technologies available combined with a deep operational understanding of the processes involved in compliance workflows is often all that's needed to create a solid digital transformation roadmap. Finding the right technology partner can also help to accelerate and de-risk the innovation process, especially if your company does not have experience with automation technologies.

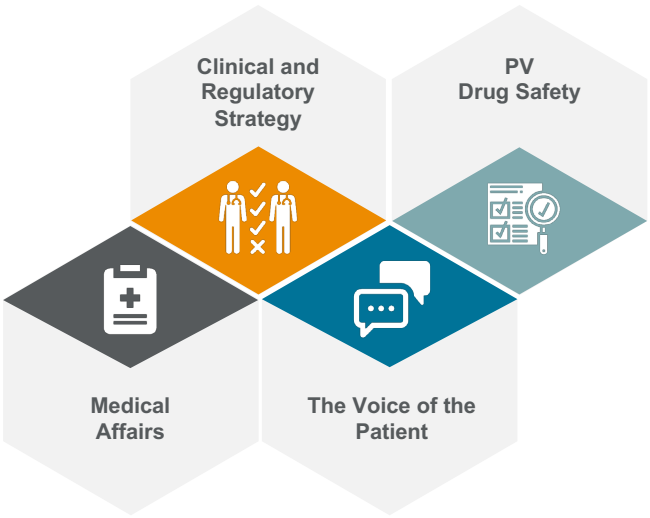
CMO Leadership and Strategy – Key to Integrated Compliance and Commercial Success

Behind any successful product launch you will find a leader who has not only helped build the scientific foundation for a product approval but one who has also provided the vision and set the tone for compliant and consistent standards needed across all medical and scientific activities. That leader is the Chief Medical Officer (CMO). The CMO provides direction for the overall clinical/scientific strategy required throughout the product lifecycle and for advancing the company pipeline. In doing so, the CMO represents the company internally and externally as the primary medical and scientific representative. This includes helping to define and develop expectations around pharmacovigilance and product safety risk management that provides for ongoing safety signal detection and benefit/risk assessment. In addition, the CMO will help to define an overall Medical Affairs Strategic Plan that supports product launch and lifecycle development and becomes the primary face of the company to the external clinical/scientific community. To achieve success, the CMO needs to be able to articulate the voice of the patient internally as the basis for decision-making when evaluating factors relevant to patients and caregivers, including aspects of quality of life.

CMO Leadership & Strategy

Provide direction for clinical strategy and for **advancing the clinical pipeline**. Represent internally and externally as a primary medical and scientific representative of the company on an interim basis

Help develop and define an overall Medical Affairs Strategic Plan and set **consistent standards** across medical and scientific activities



Help develop and define expectations around pharmacovigilance and drug safety risk management that meet standards and best practices for regulatory compliance and that **provide ongoing safety case processing** and signal detection weighing clinical benefit vs risk

Articulate the voice of the patient internally as the foundation for decision-making and when evaluating factors relevant to patients and caregivers, including aspects of **quality of life**

Medical Affairs – A Product Launch Strategic Imperative

Medical Affairs is a critical part of the strategy that helps companies ensure the successful launch of their new drug, biologic or medical device. With new product launches failing to meet corporate expectations, many companies are increasingly turning to their Medical Affairs teams to meet this challenge because they add important value through the engagement of key stakeholders in scientific information exchanges conducted in non-promotional contexts. In the age of Big Data, digital technologies, complex personalized approaches to medicine and real-world evidence generation, healthcare providers are finding it increasingly difficult to navigate the vast amounts of data needed to make the best therapeutic decisions for their patients. Medical Affairs teams equipped with extensive product and disease knowledge are well-positioned to be the conduit by which this data, along with fair and balanced scientific evidence and insights, is communicated, providing healthcare professionals and payers information needed to make informed decisions.

Companies also realize that interactions with healthcare professionals, payers and key opinion leaders provide important opportunities for insight generation that can inform market potential and patient needs, target product profile gaps and yield a better understanding of the competitive landscape. These valuable insights inform the design of clinical programs and real-world evidence generation in support of product life cycle development.

When formulating a Medical Affairs plan, a comprehensive and well-designed strategy is necessary to address key business questions and successfully commercialize a brand **(FIGURE 4)**.

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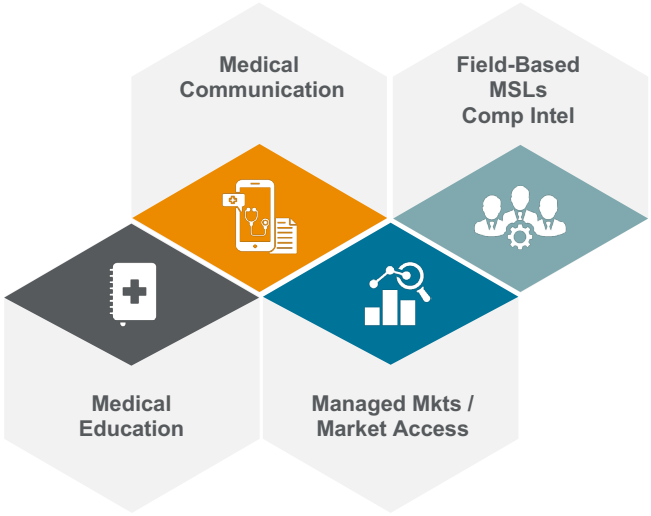
Medical Affairs Strategic Plan – Key Business Questions

FIGURE 4

How will you respond to unsolicited requests for information from HCPs, **patients and consumers concerning the safe and effective use of your product**?

How will you educate physicians and other key HCPs about the overall place of your product in **treatment in order to drive adoption**?



How will you engage KOLs and bring field-derived medical insights back to your company in order to **integrate this information with key messaging**, clinical trials and real-world evidence?

How will you respond to payer needs for comprehensive information about your product in order to make formulary decisions **while meeting regulatory requirements**?

A well-designed Medical Affairs plan has become a product launch strategic imperative and generally includes the following:

1. Medical information contact/call center support responding to unsolicited request for information
2. Field-based medical science liaisons, advisory boards and speaker programs
3. Congress planning, support and participation
4. Scientific content development, publications and publications planning
5. Managed market/market access and compendia listing support
6. Grant review and support for independent medical education and investigator-initiated trials
7. Health economics outcomes research and real-world evidence generation

Medical Affairs teams are well-positioned to engage healthcare professionals and payers in scientific discussions that clarify product benefits and risks and drive early adoption. Leveraging the full potential of a Medical Affairs team is no longer an option, but a requirement for successful commercialization.

Medical Information Contact Center: Key to Successful Pre- and Post-Commercialization

The Medical Information (MI) Contact Center provides a communication channel with the healthcare professional prescribing and recommending the product to patients and with consumers who are interested in receiving more information regarding the product. Most Medical Affairs Strategic Plans include preparing

the MI Contact Center to address unsolicited medical information inquiries post-launch. We recommend establishing a live contact center prior to commercial launch to add greater value to key customers by providing early access to information and insight about the product or disease state. The MI Contact Center provides important product launch information and can assist with the recruitment efforts of ongoing clinical trials. In addition, the MI Contact Center can be an access point in providing information on any compassionate-use and expanded-access programs prior to product launch.

When considering an integrated structure for supporting a product launch, the MI Contact Center plays a central role by establishing a well-defined and seamless workflow between the center and any patient services or hub support contact centers. This integrated approach increases successful customer experiences while maintaining compliance and provides customers a clear route to report adverse events and product quality complaints.

In addition, the system integration of sales customer relationship management platforms with the MI system is essential to ensure a direct channel for healthcare professionals to receive important information to unsolicited inquiries, especially for providing information that is not addressed in the product labeling (off-label information).

Selection of a robust and compliant MI system is paramount to the success of an MI Contact Center operation. Detailed and strategic collection of information from MI interactions will provide valuable data and metrics to inform a unique narrative of the product usage, safety profile and considerations from customers. The MI system must also establish that full compliance measures, including those that meet GxP regulatory compliance and FDA's 21 CFR Part 11 requirements, have the ability to establish country-specific data privacy rules for considerations of HIPAA and GDPR as well as reporting features to meet Sunshine Act reporting needs. Finally, the MI system needs to have an intuitive user interface to allow the MI specialists to perform their tasks with ease so they remain focused on providing the highest-quality service and delivering the best customer experience.

MI is a key customer-facing unit of the product brand, and the MI contact center must embody a strong culture of service to ensure the highest-quality response to medical and clinical inquiries with a steadfast focus on the patient. This translates to every MI specialist understanding that each MI interaction with a customer is another opportunity to demonstrate this value.

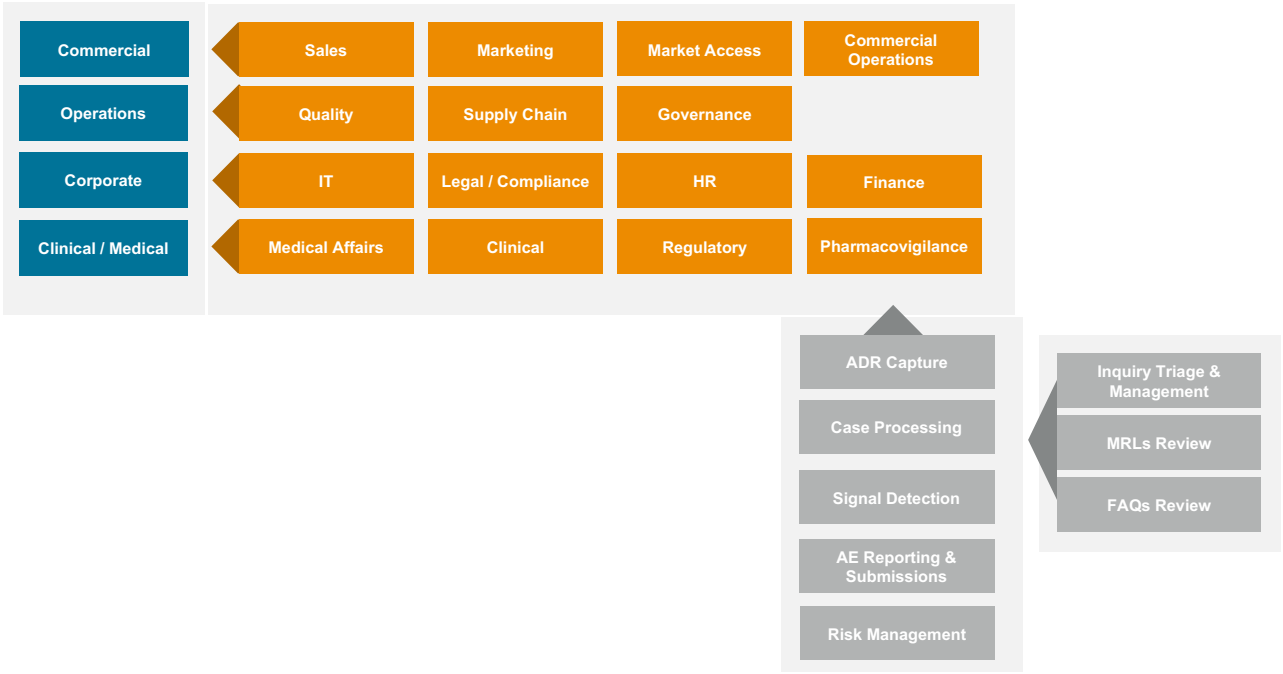
Pharmacovigilance: Product Launch Critical Success Factors

Managing the safety profile of a product is key to the overall compliance strategy for an organization looking to launch a biopharmaceutical product. A pharmacovigilance (PV) plan and execution strategy that incorporates all aspects of the product's safety profile provides the strong foundation for an effective and efficient approach that also meets all compliance requirements.

Implementing the PV plan includes detailed step-by-step tactics on who will manage the following responsibilities: what will be managed within the organization vs. outsourced, what oversight will need to be in place for any outsourced activities, and what systems will be utilized for safety reporting and managing safety trends. It must also provide details on how the plan and systems will meet the requirements for all countries targeted for product approval. The PV plan needs to efficiently and seamlessly coordinate all safety activities across medical information, quality management and regulatory affairs functions successfully in order to drive the goal for 100% compliance.

FIGURE 5

Integrated Pharmacovigilance Strategy



A robust PV plan not only allows for a review of a product's safety at key post-launch milestones but also includes an ongoing safety monitoring plan to evaluate any potential trends to proactively take action as needed for Commercial and Medical Affairs teams.

To achieve a successful product launch and subsequent commercialization, the PV plan should include:

- A thorough process for documenting and reporting adverse events per country-specific regulations and/or guidance.
- Clear channels for reporting safety events from any source, including reconciliation with these sources.
- Distribution of safety information to the required parties for awareness and/or action, considering any in-license/out-license asset agreements for safety data exchange.
- Ability to scale up resources for safety management due to unforeseen circumstances, i.e., product recalls or product withdrawals.
- Accurate and current information for product safety that is captured in validated safety systems to allow the data to be reported in health authority databases.
- Signal detection and evaluation plans for trending of any potential safety concerns as part of ongoing review of safety profile that can impact product label.

Quality Assurance: Differentiating Product Launch Success

The ability to identify the appropriate quality and regulatory strategy early in the product lifecycle provides the appropriate scope and framework to reduce time, regulatory/business risk and overall cost to launch – key differentiating factors for a successful commercialization. Some high-level Quality Strategy elements needed to achieve the key ROI and major benefits, indicated in **FIGURE 6**, include:

- Company goals and structure.
- Outsourcing strategy.
- Exit or growth strategy.
- Intended market.
- Product type and classification.
- Regulatory strategy and overall route to market.
- Intended launch timeline.
- Pre-market and post-market tactics.
- Implementation, execution and maintenance.

FIGURE 6

Manufacturers are well aware that the costs of noncompliance can be significant and compounding. Many of the serious challenges below can either delay or derail the commercialization of a product:

1. Rejected product and/or adulterated product leading to complaints, leading to adverse events, leading to recall and agency action
2. Remediation of agency action ranging from the hundreds of thousands of dollars to millions of dollars
3. Product recall and remediation never planned or staffed for; significant internal and external resource burden required

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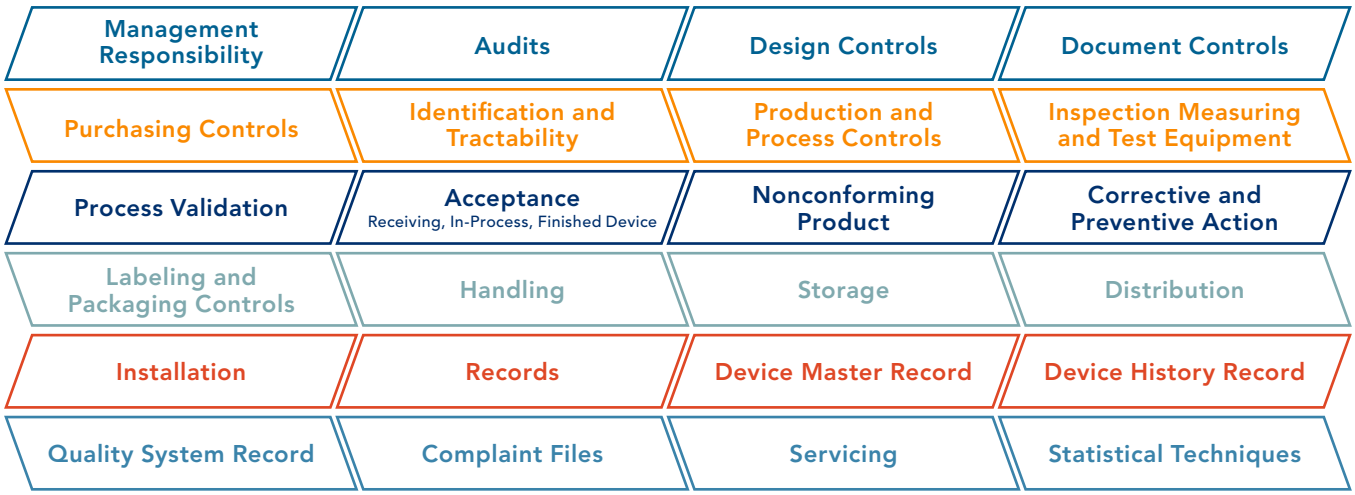
To cover the elements of quality for a medical device, pharmaceutical, biologic, tissue or combination product, it is important to establish a Quality Management System (QMS) that outlines and governs each element as it relates to the company and the product.

A phased approach to this implementation or the implementation of key elements as they become relevant/required should also be part of the overall Quality Strategy. The chart below highlights many of the elements critical to success.



Having access and control of the QMS is essential for any size business. Selection of the appropriate eQMS software should also be identified during the Quality Strategy process. Selecting the right platform for the overall company strategy and future state is crucial to short- and long-term success. Software can be a great tool in this area, or it can become a burden if not understood and is sized only for the task at hand.

Establishing a strategy is a great start to kicking off the Quality Assurance program; however, vision without execution is just a hallucination. EVERSANA supports not only the development of the quality strategy but execution of all activities required to run a successful quality department. The above elements – Quality Strategy, Quality Management System and Quality Management Software – should be acknowledged early to achieve successful commercialization. As part of an integrated compliance model, addressing these challenges helps clients realize the full value of their products at launch.

Regulatory: Critical Milestones for Successful Commercialization

There are many regulatory factors to consider in successfully launching a product. These factors could be considered the "pillars" of regulatory launch readiness, and within each of these pillars are various activities and milestones that must be achieved. The six key pillars are below; and for this white paper, we'll address the first two:

1. **Regulatory strategy**
2. **Regulatory project management**
3. **Product label management**
4. **Regulatory intelligence**
5. **Submission management**
6. **Registration management**

The key to properly addressing a regulatory strategy that supports product development is to start early – years before expected product approval. This strategy should be written to address product launch and post-market necessary cross-functional areas, such as reimbursement, marketing, legal, etc.; so when product launch is imminent, those ancillary factors are accounted for. It is important to note that the regulatory strategy is a living document; and as policy, regulations and guidance evolve, so must the regulatory strategy. An out-of-date regulatory strategy is catastrophic to product launch.

As timing of product launches becomes increasingly more critical, it's imperative to develop the regulatory strategy to eliminate these timing risks. The strategy must include establishing positive and constructive relationships with the review team so that when the product is under review, the team is more collaborative – positively impacting the timeline. Additionally, be sure to take into account any specialty programs or designations that may be applicable to the product, such as orphan designation, fast-track designation, breakthrough designation, RMAT designation or accelerated approval. These designations facilitate streamlined development and review timelines, given options for rolling review and priority reviews.

Regulatory project management cannot be overlooked, as this pillar is responsible for establishing critical internal processes and systems to support everything from the marketing application to post-market program maintenance. Comprehensive timelines and project plans defining key activities, assignments, deadlines, milestones, etc., need to be developed. A system should be established to ensure that both internal and external communications regarding the product are defined and controlled. This system needs to take into account laws and regulations, such as the False Claims Act, Anti-Kickback Statute and the Health Insurance Portability and Accountability Act (HIPAA). The Target Product Profile (TPP) must be developed and finalized to be the foundation of subsequent label and labeling development.

Additionally, establish a system to set up a promotional material review committee (PMRC) or equivalent, as well as a process for submission of promotional material to the regulatory authorities as appropriate. The PMRC should comprise various relevant functions, such as regulatory, clinical/medical, commercial, marketing, operations, etc. Ensuring cross-functional review and approval is critical to not only compliant product labeling but also product labeling that will differentiate the product from its competition and/or properly communicate the product's value to patients and providers at product launch and throughout commercialization.

Regulatory is a major component of an integrated product launch solution. A deficient regulatory strategy can single-handedly derail a product launch and/or compromise prosperous commercialization, and it's critical to ensure the regulatory factors are identified, addressed early on and updated throughout development to account for the ever-changing global regulatory landscape.

Conclusion

Advancing Life Sciences Compliance to Deliver Safer Products

In building an integrated compliance platform that moves the needle of compliance from cost center to value center, EVERSANA has addressed the market dynamics that challenge clients' ability to provide real insight to products, innovation and patient centricity. Integrating processes, technology and people is essential for successful commercialization and leads to increased efficiency, reduced costs, reduction in manual errors, faster processing time and, ultimately, increased safety, quality and compliance. EVERSANA's holistic model advances life sciences compliance to deliver and commercialize safer and better products, allowing customers to stay focused on what matters most: helping patients live healthy lives.