Global Regulations Becoming *More* Uniform

Pharmaceutical companies must navigate a changing regulatory environment both here and abroad.

As the digital age brings the clinical world closer together and research and development become more global, the industry needs to find a way to address regulatory requirements across myriad regions. The global regulatory environment is getting more rigorous, and regulators around the world are collaborating more closely.

According to a survey by KPMG, regulatory issues are top of mind for industry executives. In the near future, companies plan to focus energy most on navigating the regulatory environment and investing in organic growth. Executives also say they are grappling with the constraints and complexity of an evolving regulatory environment. In fact, 60% of survey respondents view regulatory and legislative pressures as the top growth barrier for their company in the years ahead.

"There will be a significant paradigm shift in the next decade," says David Rear, president of Advance Clinical Concepts. "Despite the fact that all regulators worldwide share the same aim — improve patient outcomes — we can't seem to approve drugs in different countries at the same time because of varied regulatory bodies."

At the same time, the world is shrinking, he says.

"We may see a more unified global approach toward approvals," he says. "The benefit to patients is clear: no matter where they live, medicines will someday become available under a more commonly defined objective. We're moving toward that aim. For example, the healthcare infrastructure in the United States is beginning to mirror the European market. Discussions are taking place regarding the need for active comparators in regulatory submissions and the concept of comparative effectiveness is not far behind. Of course, we're still years away from this prediction, but we will continue to see an increase in these common themes among regulatory bodies across the globe."

Regulatory dynamics have evolved significantly over the past decade as a result of the shift in market filing strategies, says John Lawrie, director of Vault Submissions at Veeva Systems.

"The financial opportunities associated with a global strategy have focused sponsors on casting an ever-growing web of globally dispersed innovation partners, operations partners, affiliates, and distributors as they seek to expand market share," he says. "This shift has inherently complicated the regulatory compliance hurdle, which sponsors must navigate effectively and efficiently to meet aggressive corporate growth goals."

There is a need for an integrated regulatory function that can proactively watch regulations in multiple markets and make the right forward-looking predictions regarding R&D regulations, says Nagaraja Srivatsan, senior VP and venture partner at Cognizant.

"Many life-sciences regulatory functions are geography based and siloed," he says. "This will limit their ability to be nimble to the changes in the international regulatory environment."

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> **JOHN LAWRIE** / Veeva Systems

International courts, as well as public opinion, favor the creation of more uniform regulatory standards globally, Mr. Srivatsan says.

"There is a need to create uniform global regulations that would be a baseline to govern the conduct of pharmaceutical companies regarding safety, disclosure, and efficacy of drugs regardless of the country they are being marketed in," he says. "Voluntary adherence to a firm set of global guidelines may lower regulatory barriers in certain emerging markets and reduce the risk of exposure to lawsuits filed against companies in their home countries."

Marc Hoffman, M.D., senior VP and general manager of biopharmaceutical development for Theorem Clinical Research, says hav-

Greatest Regulatory Concerns

Government pricing and report	43%
U.S. reform taxes/fees on industry	40%
Price controls	36%
Good manufacturing/clinical practices	33%
U.S. Sunshine Act	22%
U.S. class action suits	20%
Salesforce marketing compliances	19%
Foreign Corrupt Practices Act	9%
U.S. support for whistleblowers	6%

Source: KPMG

ing a global regulatory strategy, while desirable, is not achievable in the foreseeable future given the disparity of regulations and processes currently in place around the globe.

"In fact, we have a well-established framework for this — ICH — and the major architects of this framework, namely the FDA, EMA, and PMDA, are not harmonized," he says. "What is more likely is a continual convergence of rules and regulations as regulatory bodies continue to streamline their processes to take advantage of prior data that has been generated while ensuring that they are safeguarding well-being for their respective populations."

Mr. Srivatsan says barriers may be eliminated by creating multi-country regulatory boards with reciprocity agreements that may help expedite approvals of products across broad geographic regions — as opposed to by country — by developing and agreeing upon standards that all member countries can agree upon or by fast-tracking products already approved in member countries.

Mr. Lawrie says at the heart of regulatory compliance is the tracking and dissemination of regulations and commitments made in each local market.

"A critical element in maintaining compliance is the technology infrastructure that supports this management and consumption of information across a sponsor's global network," he says. "The inherent complexity, scalability challenges, and maintenance costs associated with client/server architectures are well-known and lamented. A bricks-and-mortar mindset to systems consumes a sponsor's resources and restricts the pace at which companies can grow."

Mr. Lawrie says cloud systems are inherently collaborative by nature and can both simplify and enhance a sponsor's ability to track and communicate compliance matters within their network of affiliates, distributors, and partners.

"By embracing these technologies, sponsors are more nimble while the requisite compliance and communication backbone scales fluidly and behind the scenes," he says.

Over the last 25 years, probability of regulatory success has evolved from a second thought to the forefront of drug development, says Craig Audet, Ph.D., senior VP, operations and head of global regulatory affairs at Arena Pharmaceuticals.

"Ten or 15 years ago, it was the exception to assign a no-go development decision to a promising drug candidate based on regulatory approval concerns," he says. "Nowadays, it is commonplace and often takes precedence over the science of the drug discovery."

As a result, Dr. Audet says, many compounds that have the potential to have a beneficial effect on the lives of patients are relegated to the shelf rather than the pharmacy.

"The current tendency of regulatory professionals to acquiesce to health authorities' demands rather than think out-of-the-box and work with them to establish a development plan that is thorough but also reasonable is a major impediment to growth," he says. "This way of thinking requires a new breed of regulatory professional who will avoid the tendency to acquiesce to drug development based on following the mantra espoused by the plethora of guidance documents rather than using all of the resources at their disposal as tools toward developing a thought-provoking dialogue with regulators. In my experience, building relationships, taking a science-based logical approach, using a collegial rather than adversarial style, and establishing regulation communication make a significant difference."

> **"Healthcare reform regulations put a significant financial strain on the industry and its current process for the determination and management of a variety of out-of-pocket expenses."**
>
> **PAUL KANDLE** / OPUS Health

U.S. Healthcare Reform

After three-plus years and many attempts to repeal it, one of the Affordable Care Act's major provisions went into affect. Health insurance exchanges, the backbone of the law's coverage expansion, began enrollment in October, with coverage going into effect this year.

According to PwC, the impact of this will not be as significant for pharma as it will be for insurers and hospitals. Any gains in increased sales will likely be offset by new rebates and discounts the industry is required to pay. In fact, branded pharmaceutical could potentially lose about $155 billion over the next decade as a result of discounts in the Medicare Part D doughnut hole, increased Medicaid rebates, fees, and the establishment of a biosimilars regulatory pathway.

PwC executives say healthcare reform changes will exposure medicines to greater scrutiny. Four-fifths of the U.S. health insurers polled by PwC in a recent survey now require evidence of cost savings or a clear clinical benefit to include new products in their formularies. And 16% have also entered into outcomes-based contracts with pharma companies, while another 33% expect to do so within three years.

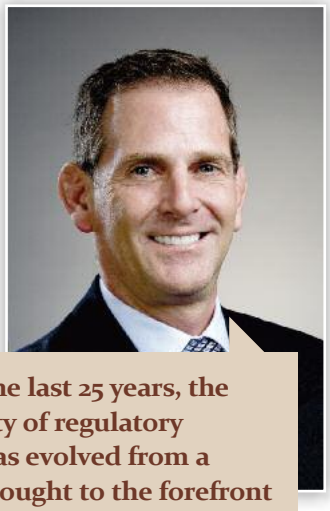
The Asian Market

The heterogeneous and fast-evolving healthcare policy and regulations across Asian nations have posed new challenges for countries looking to access markets in Asia, says Kevin Lai, director of biomedical sciences and consumer businesses at Singapore Economic Development Board.

"Beyond traditional developed markets, companies would have to cater for Asia in their global development plans in order to be competitive," he says. "In Singapore, we see the trend of companies developing strategic regulatory teams in Asia in order to better respond to changes, plan the pan-Asian regulatory strategies, and to co-develop global strategies. It is also important for companies to engage with regulators early on, especially for new technologies and modalities that they are not familiar with.

Mr. Lai says looking forward, Asia's healthcare markets continue to evolve rapidly from a policy and regulations standpoint, all segments of the business will be affected. For companies to achieve effectiveness in market access, they must be able to react quickly to these changes.

"We believe that an integration location with commercial, R&D, and manufacturing activities will allow key company decision makers and commercial leads to adapt quickly to market needs," he says. "For example, the commercial teams should channel market insights and demand sensing information more quickly to their supply chain and clinical development so there is a shorter lag time."



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> **DR. CRAIG AUDET**
> Arena Pharmaceuticals

Paul Kandle, VP and general manager, OPUS Health, a division of Cegedim Relationship Management, says healthcare reform regulations put a significant financial strain the industry and its current process for the determination and management of a variety of out-of-pocket expenses.

"We can address these potential issues by being proactive and innovative in our approach by changing the current model, and we need to be progressive in our thinking," he says. "What may have been effective in the past may no longer be the case, and we need to develop a variety of solutions that can be leveraged as the ACA becomes more clear."

Life-sciences companies need to prepare in the coming years for increased pricing scrutiny and pressures, Mr. Srivatsan says.

"Life-sciences companies need to prepare themselves on how they are going to articulate the overall cost value of their drugs in terms of the benefits they deliver to the overall health of the individual rather than just the cost of the treatment," he says.

Other Regulatory Challenges

David Shoemaker, senior VP, R&D, Rho CRO, says the Breakthrough Designation implemented as a result of the Food and Drug Safety and Innovation Act (FDASIA) will have the longest lasting impact on product development practices and timelines if the FDA funded sufficiently to enable it to implement it effectively.

"Companies are already proposing the FDA accelerate the interaction between the agency and industry by abandoning PDUFA requirements for formal meetings for products obtaining Breakthrough Designation, which would demonstrate the marked acceleration of development," he says.

> **"Increased interaction between the FDA and the industry during the marketing application review period implemented as a result of FDASIA will demonstrate its benefits over the next year."**
>
> **DAVID SHOEMAKER** / Rho CRO

Mr. Shoemaker says the increased interaction between the agency and industry during marketing application review period implemented as a result of FDASIA will demonstrate its benefits over the year and determine if its ultimate goal of achieving a higher rate of first review approvals is obtained. PV

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